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CINEROENTGENOGRAPHICALLY DEMONSTRATED CHANGES IN THE FETAL CIRCULATION OCCURRING AT BIRTH*

A SERENDIPIC COMMENTARY

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It is an honor, however undeserved, for me to be asked to give the fifth W. Edward Chamberlain Lecture. It has not been my privilege to know Dr. Chamberlain until today, although the nature of his contributions to radiology reached even my distant ear some years ago upon his appointment to the Chair of Radiology at Temple University. My ear was distant not in space, for he became Professor of Radiology here at Temple University while I was still a graduate student at the University of Pennsylvania, just across the city. It was distant because my interest in basic medical science was far removed from the need for using radiologic techniques. How many endocrinologists, physiologists or embryologists have more than a nodding acquaintance with the uses of such tools for investigation? I was one of a majority, I am sure.

There came a time, however, when it became necessary for me in the course of my work to know how rapidly the blood flows through the pregnant uterus of the intact monkey. What better way to learn this than to propel some opaque medium at high speed through the linea alba, into the myometrium, and then observe how rapidly this was removed? To use isotopes would have left traces of radioactivity in tissues other than the myometrium, but roentgen rays offered the opportunity to localize the injected substance within the myometrium. We conducted a little study of this problem[1] and proved the feasibility of this technique (Fig. 1).

Even so, I did not even then learn first hand of Dr. Chamberlain. It really was not until I came to Temple University two years ago as one of a group of NIH consultants that I learned of the impact that he had made upon this institution. I found that here advanced radiologic techniques are used for research and teaching in the Departments of Physiology and Pharmacology as well as in Radiology. Here, these techniques are wisely and extensively employed. Of course, Dr. Stauffer and others have implemented such activities far beyond what Dr. Chamberlain did, but there is no doubt that Dr. Chamberlain has left here an intellectual legacy which is strong, growing and evident.

When Dr. Oppenheimer invited me to give the Chamberlain Lecture, I had serious doubts as to the wisdom of accepting the proffered honor. Upon consideration, however, I decided that perhaps my experience with serendipity in the field of radiology might make an interesting footnote in the annals of radiology, for it opened up avenues of investigation along which I have moved for ten

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The W. Edward Chamberlain Lecture, delivered at Temple University School of Medicine, September 29, 1960.

years, and I presume I shall continue, with good fortune, to move along them for some few years to come.

SERENDIPITY, the gift of finding valuable and agreeable things not looked for, is a word coined by Walpole in allusion to a tale, *The Three Princes of Serendip*, who in their travels were always discovering by chance or sagacity, things they did not seek. My tale of serendipity goes back to my laboratory in Baltimore in 1948. A young doctor from Harvard came in and put on my desk some injection-corrosion specimens of the blood vessels of human placentas. He wanted help in developing a research project out of these specimens. In the course of our discussions, we noted something that no one else, especially any physiologist, apparently had observed. It was that, unlike virtually most other vascular beds, this one was unique. The cross-sectional areas of the veins were not appreciably different from the cross-sectional areas of the arteries that supplied the substance of the placenta. This being so, it readily suggested to us that the velocity with which the blood moves through the veins necessarily must be close to that at which the blood moves through the arteries.

From a physiologic standpoint this presented a dilemma. The blood in the arteries moves into the placenta under considerable pressure from the heart. But how about the pressure of blood in the veins? Where did the energy come from to propel the blood through the veins at as high a velocity, back toward the heart? It also raised the question of how much energy is lost against the vessel wall by blood flowing through a

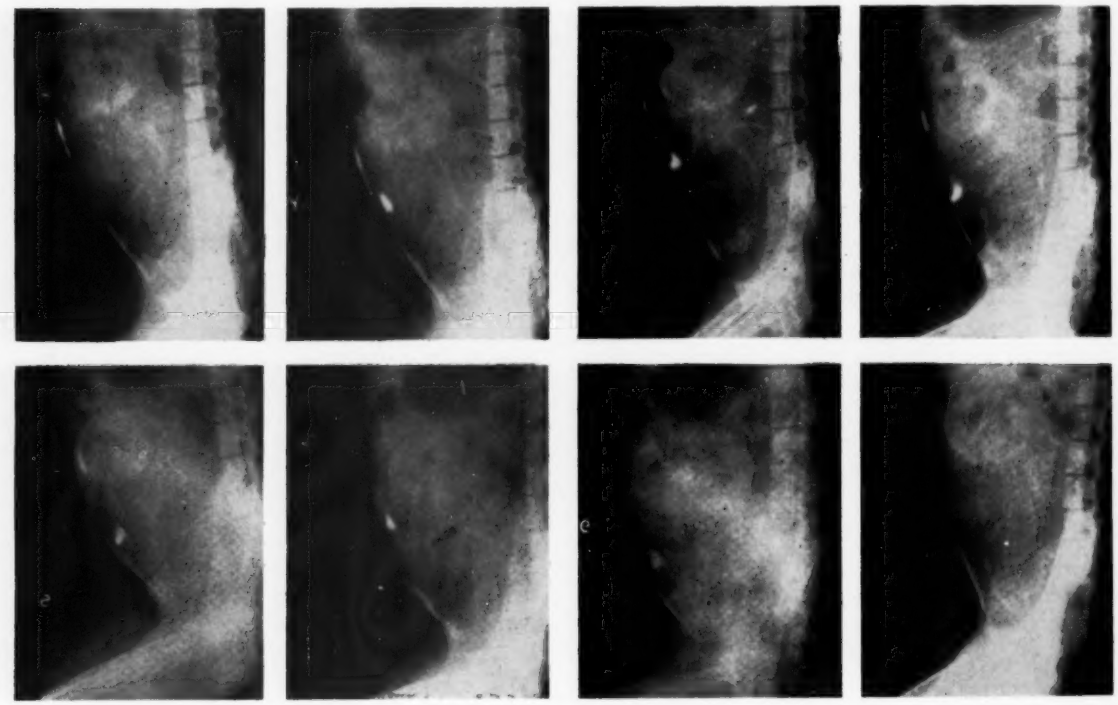

FIG. 1. Roentgenologic determination of an index to the blood circulation time in the intact uterus of a monkey pregnant 106 days. By jet hypospray, 1 ml. of diodrast is propelled through the linea alba into the myometrium. A residue from a previous injection of 1 ml. into the rectus abdominis muscle is seen in top left. Next right, 10 minutes later, the contrast medium had just reached the uterus. Succeeding roentgenograms were taken at regular intervals until both areas cleared. Twenty-four minutes were required for clearance in the the rectus abdominis, 34 minutes for the uterus. (Reproduced with permission from the *Proceedings of the Society for Experimental Biology and Medicine.*)

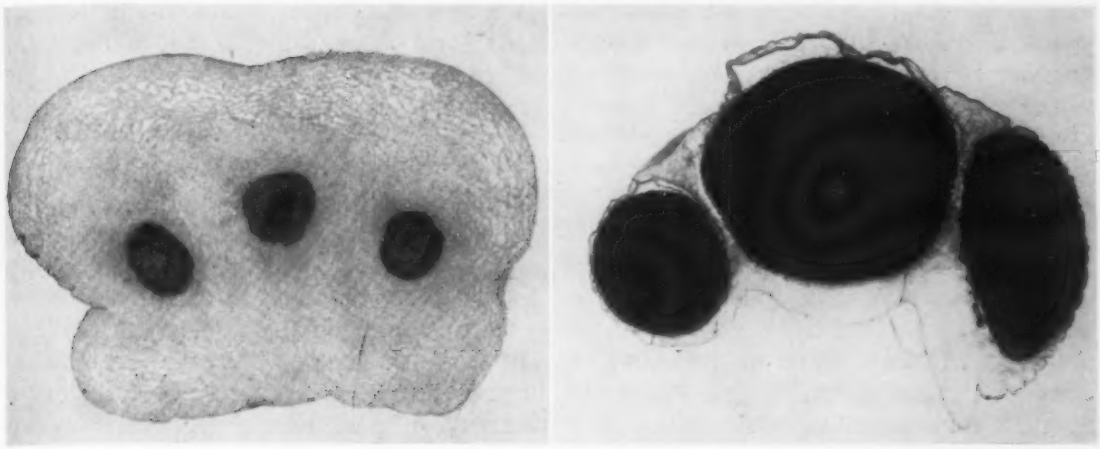

Fig. 2. Two sections of an umbilical cord. Left: conventional section with the two arteries and vein constricted and empty with much Wharton's jelly present. Right: section of the same cord taken with the infant held at the level of the placenta *in utero* and with two clamps placed simultaneously on the cord with a full pulsating beat. Note the large, distended vessels, the thin walls of the blood vessels and the thin layer of sheath about the cord. Wharton's jelly piles up as the cord shortens with vasoconstriction. (Reproduced with permission from *Contributions to Embryology*.)

vessel, and how much by internal dissipation of energy through the viscosity of the blood? Since the placenta seemed immune to *in vivo* experimental investigation, it occurred to me that perhaps this could be studied in the umbilical cord. The only difficulty was that histologists always study a cord after it is cut, with the blood drained out of it and the vessels constricted. Clearly, there had to be a way to determine the cross-sectional areas of distended and functioning umbilical arteries and veins.

I then went to a colleague in the Department of Obstetrics and asked him: Would you between the second and third stages of labor hold a baby at the level of the placenta, still retained within the uterus, and, with a full pulsating beat in the cord, put two clamps simultaneously at different points on the cord and then remove the distended segment?" This he did, whereupon I fixed the segment, with the clamps still on it. The result,[5] which was repeated many times, is shown in Figure 2. Here it was found that the combined areas of the two arteries were some 80 per cent of the area of the vein. So it was true that the blood in the vein moved only about 25 per cent slower than in the arteries. The functioning umbilical cord was clearly the tissue to be used to study the problem we had posed for ourselves, but where should we go from here?

I went to the Department of Sanitary Engineering at Johns Hopkins to talk to a colleague about our worries. He was a man noted for having successfully designed sewer systems for various towns and cities in the United States. Surely, I thought, he would know about fluid flows, and he could help me design an experiment to solve our problem.

Dr. Guyer was very helpful. What we would need, he said, was knowledge of the pressure drop along a length of blood vessel, the velocity of blood flow, the volume of blood flow per minute, and the amount and form of expansion of the blood vessel with each heart beat, since a blood vessel is nonrigid. We would need to know *all* these things simultaneously, and in one experiment!

There was but one place at that time where I could do this work—the Nuffield Institute for Medical Research, in Oxford, England. The reason for my selecting Nuffield Institute lay primarily in the fact that a book had been published a short while be-

fore by Barclay, Franklin and Prichard[2] entitled *The Foetal Circulation and Cardiovascular System, and the Changes They Undergo at Birth.* The approach in this now classic book had been entirely roentgenographic. They had taken serial roentgenograms at 2–5 images a second, and had learned much that was new as well as confirming much that had been known. I would remind you that, up to 1949, almost no one had produced truly good cineangiograms and there were no image amplifiers except in experimental stages. Moreover, at that time there were no laboratories where complicated animal experiments could be done using roentgen-ray techniques. This was what took me on a wandering trip to the British Isles, and points beyond.

But what did we discover that was valuable, agreeable and not looked for? I shall not tell you all that we learned. That would require many hours. Rather, I shall dwell on only a few facts that radiology revealed.

First, however, I must pay tribute to the radiologist who came to be my colleague. He is Dr. Gordon Ardran. Dr. Ardran considered the needs of my project and concluded that serial roentgenograms at 2–5 images per second would not suit our purposes. Instead, we would need true moving pictures, at better than 16 frames per second. With the limitation of little money, but with considerable resourcefulness, he bought a discarded moving picture projector from a local theater for the sum of ten pounds, or twenty-eight dollars. This, by ingenious adaptation, was made to take direct angiograms or cinefluorograms at a speed of 25 frames per second on 35 mm. film. So here, for almost the first time, true moving pictures of events could be taken by roentgen rays under highly experimental conditions. With this apparatus our work fell logically into two programs. One, of course, dealt with the umbilical cord. However, as we took cinefluorograms of the cord, we also obtained for the first time true cineangiograms of the fetal circulation. This, under the stimulus of Dr. Marjorie Prichard, who was a colleague, became our second area of study. We had no intention at the outset of engaging in fetal studies.

We learned much about blood flow in the umbilical cord. We found, for example, that if there is stream line flow (as there is in the larger vessels of almost the entire body) outside the ascending aorta and the arch of the aorta, the blood flows with surprisingly little loss of energy. In an umbilical vessel, there is only about a 2 per cent loss of energy in the system per centimeter of blood vessel. This means that, in the sheep fetus, about 90 per cent of the energy in the aorta is available to propel blood through the umbilical arteries.[9]

We[6] learned, too, that there is an advantage to an organism in having a blood vessel over a given diameter in order that it conduct blood efficiently (Fig. 3). For example, when a vessel has a diameter of 2–3 mm., the flow was 5–6 ml.[3] per second. When, however, the diameter was 3.4 or

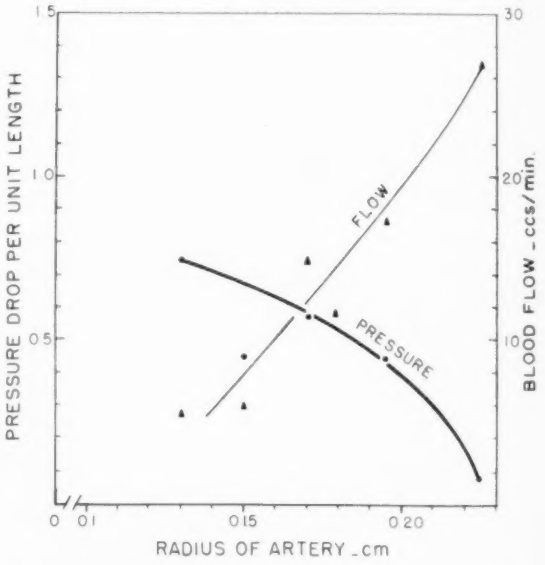

FIG. 3. Graph showing data obtained by cineangiography on the relation between the diameter of an umbilical artery and the flow of blood. The flow increases as the diameter increases; the pressure falls, as shown. (Flow is in ml./sec.) (Reproduced with permission from the *American Journal of Obstetrics and Gynecology.*)

4.0 mm., the flow was 15 and 17 ml.[3] per second, respectively.

The basis of these figures rests on the analysis of cineroentgenograms taken at 0.04 second. We could tell how many frames were required for the velocity-head of the opaque medium to traverse a given distance and we could, allowing for parallax, measure very well the diameter of the vessel studied. From these simple facts, unobtainable in any other way, we established these figures which any physiologist could have reasoned ought to apply, although he would not know what values to assign to the situation.

I have said that I went to Oxford to study hemodynamics in the umbilical cord. I have also noted that in so doing, we could not help but cineroentgenographically record the fetal circulation as well. Again we observed processes which we never anticipated might be available to us. When we saw the pictures projected, we were impressed by the fact, but hardly surprised, that we could see any major part of the fetal vascular tree. What could be simpler than to study how long a time was required for the opaque medium to pass from one part of the vascular tree to another? Thus, we could see it start toward the head in the areas supplying that region of the body, and we could see it return. Consequently, the cephalic circulation time could be measured. Similarly, the pulmonary circulation time was measurable, as were the renal, the portal, the hepatic, and the intestinal circulation times. We could even measure the length of time it took for the medium to pass down the aorta to one of the mesenteric arteries. We could—and did—measure the placental, and even the placental cotyledonary circulation times. In short, from cineangiofluorograms, we could learn for the first time what the regional circulation times in a fetus are.

Early in the study, Dr. Prichard, who had played an important role in the work on the fetal circulation, said, "I would like to see what happens when we give the fetus artificial respiration." Now, to put this in perspective, it is necessary to state what Barclay, Franklin and Prichard[2] had established earlier.

They had found that the unique features of the fetal circulation undergo profound changes and in an apparent sequence upon establishment of respiratory movements. One of these features is closure of the ductus venosus, that structure lying deep within the recesses of the liver which is the main connection between the end of the umbilical vein and the inferior vena cava. It is so well protected by soft and blood-loaded tissue that it can only be studied functionally by roentgenography. Closure of this sphincter, they postulated, prevented hemorrhage through the torn umbilical cord after birth, for most mammals at birth are unattended by an obstetrician who clamps or ties the severed umbilical cord.

The second significant change at the time of birth is closing of the ductus arteriosus which, as these authors demonstrated so elegantly, interposes a block between the pulmonary artery and the aorta after establishment of breathing, and so directs all the blood from the right heart into the lungs. The third essential change is closure of the foramen ovale, the opening in the interatrial septum that serves during fetal life to admit blood from the right to the left side of the heart, thus bypassing the fetal lungs. In their study, it is never precisely stated what the order or sequence of closure of these structures is. It is here that, as we wandered through one experimental procedure after another, we uncovered a series of related facts of immeasurable importance to our understanding the nature of the fetal circulation and the changes it undergoes at the time of birth. We will look at these, one by one.

First, the ductus venosus. To understand this, I must narrate my talk with the engineer, Dr. Guyer. When I talked to him, he asked about the pressure in the umbilical vein (which I knew to be high) and how the vein ended in the liver. I sketched for him the umbilical recess in the liver, showing

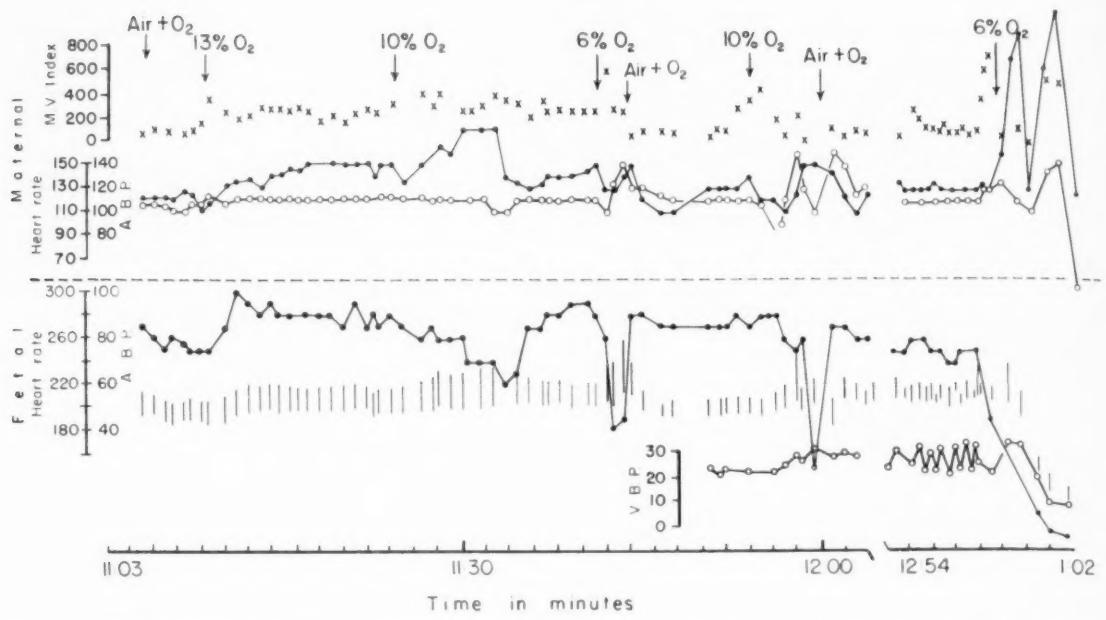

FIG. 4. Graph showing the effect of umbilical vein pressure on the welfare of the ewe fetus *in utero*, with the membranes intact, during severe hypoxia. Events in maternal ewe (top): respiratory minute volume index, x; heart rate, o; mean carotid blood pressure, •; in the fetus (bottom): umbilical artery pulse pressure, |||; umbilical vein pressure, —. Note that on 13 per cent and 10 per cent O_2 is ewe's inspired air; fetal heart rate was variable as arterial pulse pressure improved. Venous pressure held constant at 20–28 mm. Hg. On the second exposure to 6 per cent O_2, maternal hemodynamic disturbances occurred and the heart rate fell, as before; venous blood pressure fell (with probable closing of the umbilical vein) and then arterial pressure fell. The fetus died.

the ductus venosus as a wide, open structure passing into the inferior vena cava, and many small tributaries going off into the substance of the liver. He put his pencil on the ductus venosus and said, "Where is the valve here that controls the pressure back here in the umbilical vein?" I said, "There is none." He said there had to be. Then, recalling that there is a sphincter in the ductus venosus as was shown both roentgenographically and anatomically by Barclay, Franklin and Prichard,[2] he told me that hemodynamic pulsations in the umbilical arteries exerted intermittent pressures on the distended vein, and so "milked" the blood in a forward direction toward the heart. It was, he said, a pulsameter pump such as is used in the chemical, petroleum and other industries. Now this was a new idea, that the sphincter served a vital role in the maintenance of blood flow from the placenta to the fetus, instead of merely being a stopcock to shut off a retrograde flow of blood afer the organism was born. What, in our wandering, did we find?

To be brief, we found, as had Barclay, Franklin and Prichard,[2] that the sphincter may be either closed or open during fetal life. In one fetus only in which experiments were done, it was found that the sphincter could be made to open by progressively reducing the venous return from the placenta. Before leaving this subject, it should be said that later studies in recent years have shown that if umbilical vein pressure becomes low, a fetus becomes moribund and dies. If, however, it remains high, the fetus withstands stress and is very vigorous[10] (Fig. 4).

The most dramatic circulatory change in the fetus upon aeration of the fetal lungs is in the quality of the hemodynamic change in the lung itself. It is the first and largest change to take place. Dawes[3] has shown

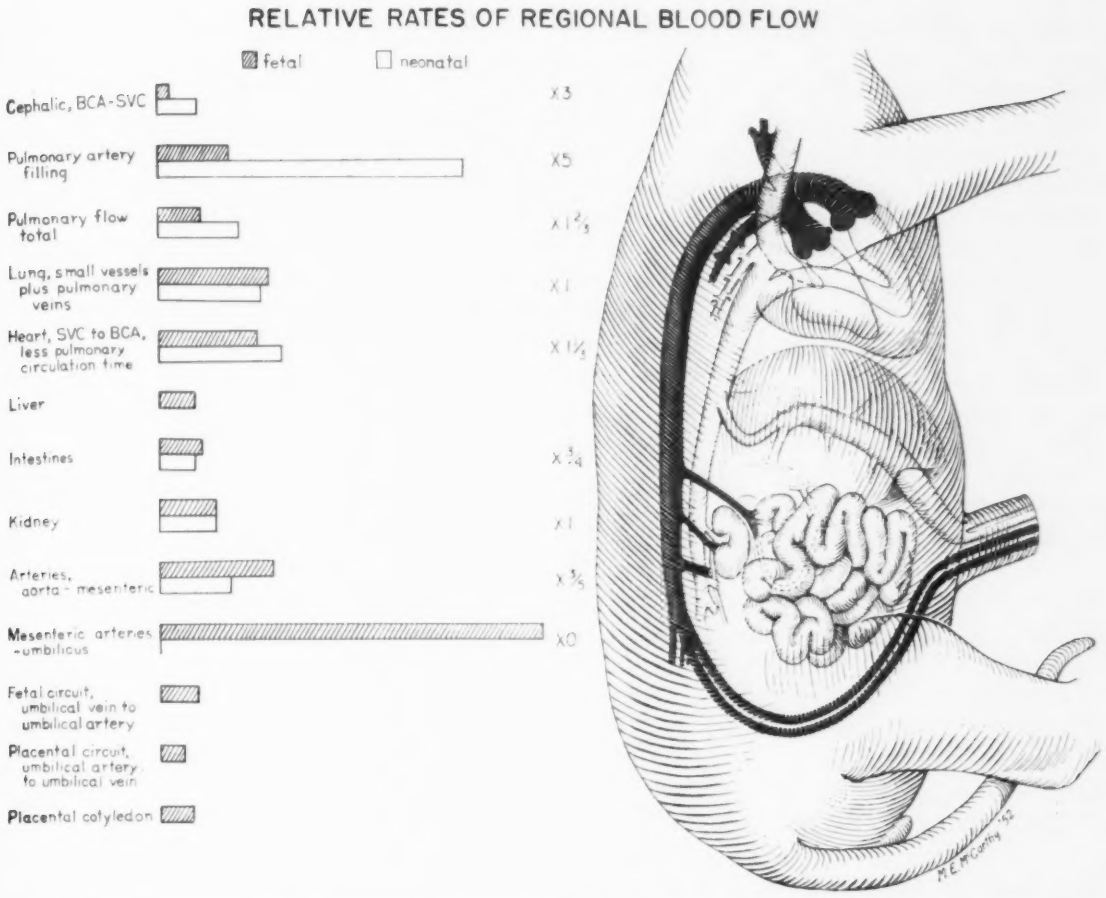

FIG. 5. Roentgenographically determined circulation times for opaque medium passing from one part of the circulatory tree to another in the fetus and breathing lamb. Cineangiograms taken at 25 frames per second permitted noting, from frames at 0.04 second apart, the transit time of the opaque medium. The spread of circulation is the reciprocal of the circulation time. The bar graphs show (fetus, striped bars; breathing lamb, open bars) that the cephalic circulation is 3 times faster after birth; the pulmonary circulation (arterial transit time) is 5 times faster, and so on. (Reproduced with permission from *Contributions to Embryology*.)

that during fetal life only about 13–15 per cent of the fetal cardiac output goes to the lung. Ardran *et al.*[1] demonstrated that the pulmonary circulation in the fetus is the slowest regional circulation (Fig. 5); however, upon aeration of the fetal lung, it becomes the fastest. This is associated with the group of physiologic changes detailed in Table 1.[7]

The cineroentgenographic demonstration of this pulmonary change, which was missed in the serial film technique, required that the anatomic nature of the fetal and

TABLE I

PHYSIOLOGIC CIRCULATORY CHANGES

Physiologic Condition	Fetal	Neonatal
Pulmonary Artery Pressure	++++	+
Pulmonary Peripheral Resistance	++++	+
Rate of Pulmonary Blood Flow	++	+++
Pulmonary Blood Volume	+	++-+++

neonatal circulations be established. This was done in 1956,[7] although to describe these results here would carry us far afield from our present theme. However, I would point out that the roentgenographic technique led inadvertently to a new line of anatomic and physiologic experiments on the nature of fetal physiology and its bearing on postnatal life.

Before concluding, some specific results of the cineroentgenographic observations on the fetal circulation should be pointed out. Careful analysis of the films showed that in the fetus circulation is slowest through the head and is slow in the lungs, liver, intestines and kidneys. The fastest and most copious flow is to and through the placenta. Upon aeration of the lungs, there is a two and one-halffold increase in the cephalic circulation, a fourfold increase through the lungs, and a complete cessation, of course, to the placenta. The flow through the heart, kidneys and intestines is unchanged. In short, Nature has contrived to have the most rapid and abundant flow of blood through the organs of respiration in both the fetus and the neonatal animal.[8] This is not unexpected, but it required cineangiography to prove the point.

I would be remiss if I did not reiterate that these initial observations have led to a succession of completed studies on fetal homeostasis, fetal distress and the life of the fetus within the uterus, with the membranes and fluid surrounding the fetus still intact. These studies have led to others which are still in active progress. It is no exaggeration to say that the casual observation of the fetus by cinefluoroangiography in the course of another study has been the most important means whereby a whole array of heretofore unsuspected problems in physiology and anatomy have come into view. In this case, serendipity has served us well.

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VOL. 86, NO. 3

THE ROENTGENOLOGIC DIAGNOSIS OF FETAL HYDROPS*

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IN A paper entitled "The Fallibility of Radiological Diagnosis of Erythroblastosis Foetalis," McClure Browne[9] states, "A radiograph of the foetus *in utero* showing the Buddha position and a halo around the skull is usually accepted as diagnostic of erythroblastosis foetalis. These signs were first described by Hellman and Irving (1938). Javert (1942) laid special emphasis on the value of the Buddha position. Ritvo, Shauffer and Krosnick (1949) claim that the signs enable a definite diagnosis of erythroblastosis foetalis to be made. Hartley (1948), however, regards them with distrust. I, too, have sometimes found these signs to be misleading, and suggest that they be valued only together with all evidence of severe foetal damage." He continues with reports of 2 cases of pregnancies producing normal babies in which an incorrect diagnosis of fetal hydrops had been based on the halo and Buddha signs.

Because of the apparent unreliability of the halo sign noted by others as well as ourselves and the diagnostic inadequacy of the Buddha position alone, we feel justified in presenting our experience with both direct and indirect roentgen signs of fetal edema. In so doing we add 4 cases to the 2 we reported in 1953.[1]

Modern methods in the care of premature infants and the spectacular results of replacement transfusion techniques make early diagnosis of this condition of great practical importance. One of our cases (Case 5) was not suspected clinically. The roentgenologic diagnosis of fetal hydrops (Fig. 8, *A* and *B*) stimulated prompt action. Cesarean section followed by immediate and repeated replacement transfusions resulted in a vigorous baby which continues to thrive. Armed with this procedure we can no longer be content to wait for "evidence of severe fetal damage" as suggested by McClure Browne.[9] Ritvo *et al.*[11] state, "as with other rare and unusual conditions, the diagnosis will be made only if the manifestations are clearly understood, constantly borne in mind and painstakingly sought for in every instance. The importance of early diagnosis in planning therapy and making a proper prognosis is self evident."

Erythroblastosis fetalis is a hemolytic clinico-pathologic syndrome of offspring resulting from conception between an Rh negative woman and an Rh positive man. The first born child is seldom affected unless the mother has previously received a transfusion of Rh positive blood. Fifteen per cent of white mothers are said to lack Rh agglutinogens and are therefore termed Rh negative. Sensitization of these mothers by the Rh positive red blood cells of the fetus causes the formation of an anti-Rh agglutinin. Erythroblastosis fetalis develops when this diffusible substance passes into the circulation of the fetus. With each succeeding pregnancy the probability of producing a baby with hemolytic disease is increased. Pickles[10] has stated that the chances of an Rh negative mother becoming immunized during the first pregnancy and therefore producing an infant with hemolytic disease are 1 in 1,000. For the second and third pregnancies the chances rise to 1 in 40 and increase to about 1 in 15 for the fifth pregnancy. Javert[7] found that the incidence of erythroblastosis fetalis after its initial appearance is nearly 50 per cent and if the first born had the disease the incidence is nearly 100 per cent. Hellman

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and Irving[5] estimate that fetal hydrops occurs once in 2,000 deliveries.

CLINICAL AND PATHOLOGIC FEATURES

The clinical manifestations of erythroblastosis fetalis fall into three groups. In order of increasing severity these are: (a) congenital anemia; (b) icterus gravis; and (c) fetal hydrops. In the mildest form, congenital anemia, the diagnosis is suspected by the pallor of the infant and confirmed by blood studies.

Icterus gravis is characterized by jaundice of varying degree that may be present at birth or may not develop for several days. The jaundice is usually progressive and is accompanied by progressive anemia.

The most severe form of erythroblastosis fetalis, fetal hydrops, is characterized by marked generalized edema of the soft parts, associated with accumulation of fluid in the pericardial, pleural and peritoneal cavities, and enlargement of the heart, liver and spleen (Fig. 1, *A* and *B*, Case 4). The blood picture is that of marked anemia associated with immature red blood cells. The placenta is large, thickened and edematous (Fig. 1 *C*, Case 4). As a result of the increased size of the fetus and the placenta, the uterine enlargement is found to be out of proportion to the duration of the pregnancy and hydramnios is generally suspected clinically. Javert[7] reports that in the 16 cases which he studied, "clinical hydramnios" was due to the combined excessive size and weight of the placenta and the infant which averaged 4,674 gm. (10.2 pounds). The placenta averaged 1,254 gm., the fetus 3,420 gm. This is a 1 to 3 ratio in contrast to the normal 1 to 6 ratio. In 5 of our cases there was a clinical diagnosis of hydramnios.

Bone changes are quite constant, occurring in the anemic and icteric forms as well as in fetal hydrops. Follis *et al.*[3] and Janus and Dietz[6] found marked increase in bone density on postnatal roentgen studies as well as on microscopic postmortem studies. There was an increase in the number and thickness of trabeculae, due apparently to lack of destruction of the calcified cartilaginous matrix substance which was then covered with a thick layer of new bone. The medullary spaces were narrowed or obliterated. In long bones a transverse zone of decreased density close to the junction of the shaft and cartilage was frequently present. This is the result of transient disturbance of endochrondal bone formation and not distinguishable from other prenatal interruptions of bone formation.

INDICATIONS AND TECHNIQUE OF ROENTGEN EXAMINATION

Indications for roentgenologic examination arise during the last two months when a pregnant woman is known to be Rh negative or has had a previous erythroblastotic baby. Hellman and Irving[5] recommend that such patients be examined every two weeks during the last two months of pregnancy. Ritvo *et al.*[11] advocate frequent reexaminations to detect early changes that might otherwise go unrecognized, the first, ten to fifteen weeks prior to term and thereafter at three to six week intervals.

Clinical suspicion of hydramnios is generally considered as a mandatory indication for roentgen examination due to the frequency with which fetal anomalies occur with this condition. Fetal hydrops must be added to the list of abnormalities to be thought of and searched for in such examinations, since uterine enlargement out of proportion to the fetal age in erythroblastosis cannot be differentiated clinically from true hydramnios.

Javert[7] found a high incidence of preeclamptic toxemia in mothers of hydrops cases (31 per cent of 16 cases). Two of our 6 cases were toxic (Table 1). Cases showing symptoms of toxemia when associated with hydramnios should be investigated roentgenographically.

Painless bleeding is a frequent symptom, occurring in 3 of our 6 cases (Table 1). The possibility of fetal hydrops must be considered in every case examined roentgenographically for placenta previa.

The technique of the examination is

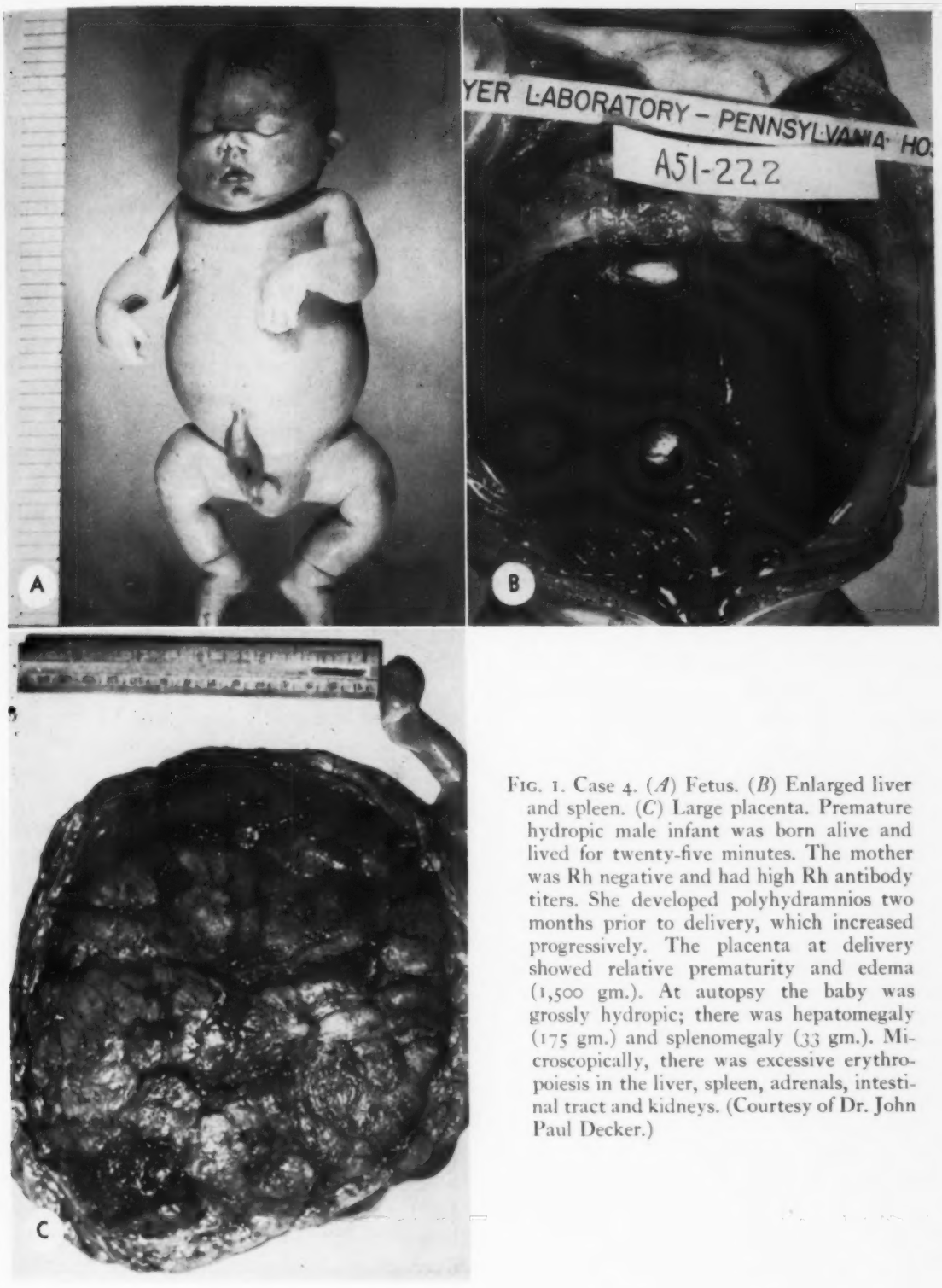

Fig. 1. Case 4. (*A*) Fetus. (*B*) Enlarged liver and spleen. (*C*) Large placenta. Premature hydropic male infant was born alive and lived for twenty-five minutes. The mother was Rh negative and had high Rh antibody titers. She developed polyhydramnios two months prior to delivery, which increased progressively. The placenta at delivery showed relative prematurity and edema (1,500 gm.). At autopsy the baby was grossly hydropic; there was hepatomegaly (175 gm.) and splenomegaly (33 gm.). Microscopically, there was excessive erythropoiesis in the liver, spleen, adrenals, intestinal tract and kidneys. (Courtesy of Dr. John Paul Decker.)

TABLE I

CLINICAL SUMMARY

Case	Hydramnios	Bleeding	Toxemia	Fetal Death	Rh	Previous Babies
1 J.W.	+	−	+	+	Neg.	Icterus gravis, Anemia
2 M.S.	+	+	−	+	Neg.	3 Normal
3 A.Y.	+	−	+	+	Neg.	2 Fetal hydrops
4 G.McA.	+	+	−	Alive 25 min.	Neg.	1 Erythroblastosis fetalis
5 C.C.	+	+	−	Living, well	Anti C factor	1 Normal 1 Icterus gravis
6 A.R.	−	−	−	Alive 2 hrs.	Neg.	1 Fetal hydrops

simple. Anteroposterior and lateral roentgenograms are made with the patient lying on a Bucky diaphragm table. High speed films and intensifying screens are used in an effort to reduce the radiation dose to both mother and child to a safe minimum. The dangers of fetal damage from repeated exposures in doubtful cases must be carefully weighed against the importance of each examination. The roentgenographic technique is of the quality used in urologic studies. Roentgenograms must be made in a minimum of time, thereby avoiding primary motion of the fetus and secondary motion of the mother. Fine detail is essential; retakes are undesirable.

ROENTGEN FINDINGS

In 1934 Snow and Powell[13] described a "black line" outlining the neck, trunk and extremities on roentgenograms of the gravid abdomen made by a soft tissue technique. This black line (Fig. 2) is due to the greater penetrability by roentgen rays of the fat containing subcutaneous tissues.[13] It was noted that it was widest over the buttocks, a notorious depository of fat, and absent over the cranium because there is no subcutaneous fat layer in the scalp. This black line, which outlines the trunk and extremities of the fetus, has become an important landmark in roentgenologic studies for localization of the placenta as well as in the diagnosis of short umbilical cord.[1] The obliteration of this fat line, secondary to edema of the soft tissues, has become our most reliable sign in the diagnosis of fetal hydrops. This corresponds to other time-proven roentgenologic changes of diagnostic importance, such as the disappearance of the shadows of the perirenal and psoas muscle fat pads in cases of retroperitoneal inflammations or tumor infiltration and the obliteration of the properitoneal fat line in patients with ascites. It should be emphasized that the fetal fat line is not obliterated when the fetus is surrounded by the excessive amount of amniotic fluid in hydramnios (Fig. 3).

In 4 of our cases prenatal roentgenograms showed the fetal fat line to be completely obliterated. In Case 5 and 6, both live fetuses, the fat line was seen very faintly along the back where the edema was less marked; it was completely obliterated over the abdomen and the extremities (Table II). In a review of the literature, roentgenograms of one case in Javert's[7] series and in 3 reported by Ritvo *et al.*[11] show the shadow of the fat line to be ab-

sent, although this finding is not mentioned in their texts. McClure Browne[9] presents beautiful illustrations of a normal case in which an incorrect diagnosis of fetal hydrops was made on the basis of the Buddha position and the halo sign. The fat line of the baby is shown with clarity. The application of our diagnostic standards would have ruled out a diagnosis of fetal hydrops in this case.

The position of the fetus in relation to the uterus is of diagnostic importance. The fetus usually lies with its back in close contact to the uterus while anteriorly the distance to the uterine wall is much greater than normal. This is due to the thickened, edematous placenta and the distended abdomen of the fetus.

The posture of the fetus is noteworthy. The ribs are elevated and in a more or less horizontal position due to the enlarged heart, the pleural fluid and upward pressure of the distended abdomen. The arms are spread outward and lie well anteriorly, displaced from the normal position of close contact with the trunk because of the soft tissue edema. The legs, likewise, assume an abnormal "frog like" position, the so-called Buddha sign. They are flexed at the knees and abducted at the hips. The extremities of a normal fetus may and frequently do assume a similar posture. This appearance, however, is important in combination with other signs of fetal edema

Fig. 2. Fat line or "black line" of subcutaneous fat surrounding the trunk and extremities of a normal fetus.

Table II

ROENTGEN SUMMARY

Case	Fetal Position	Cranial Halo	Fetal Fat Line	Bones					
				Density	Position				Cranial Bones
					Ribs	Arms	Legs	Spine	
1 J.W.	Breech	No	Completely obliterated	Moderate increase	Elevated	Out and elevated	Flexed 90° abducted	Straight	Overlapping
2 M.S.	Breech	No	Completely obliterated	Slight increase	Elevated	Out and elevated	Flexed 135° abducted	Straight	Overlapping
3 A.Y.	Transverse	No	Completely obliterated	Marked increase	Elevated	Out and elevated	Flexed 135° abducted	Increased curve	Overlapping
4 G.McA.	Vertex	No	Completely obliterated	Normal	Elevated	?	?	Straight	Normal
5 C.C.	Vertex	No	Partly obliterated	Normal	Elevated	Out	Flexed 90°	Normal curve	Normal
6 A.R.	Vertex	No	Partly obliterated	Increased	Elevated	Out	Flexed abducted	Normal curve	Normal

FIG. 3. "Black line" in a case of true hydramnios (ancephalic monster).

and enlargement of the abdomen and thorax.

The posture of the spine is of interest. Samuel and Cohen[12] state that the spine loses its normal curvature as a result of the enlargement of the liver and the spleen and ascites, but add that other intra-abdominal masses produce the same effect. Our findings are not uniform. In 3 or our cases, in which the fetus was dead and macerated, and lying in the breech or vertex position (Fig. 4, *A* and *B;* 5, *A* and *B;* and 7; Case 1, 2 and 4), there was complete absence of the normal spinal curve; 2 cases in vertex position (Fig. 8, *A* and *B;* and 9; Case 5 and 6), both alive, had normal spinal curves; another dead fetus (Fig. 6, *A* and *B*, Case 3) in a transverse lie had an exaggerated flexion curvature of the spine.

The halo sign has not been of diagnostic value in our series. Hellman and Irving[5] in their original description said, "The edema is seen in roentgenograms as a thickening

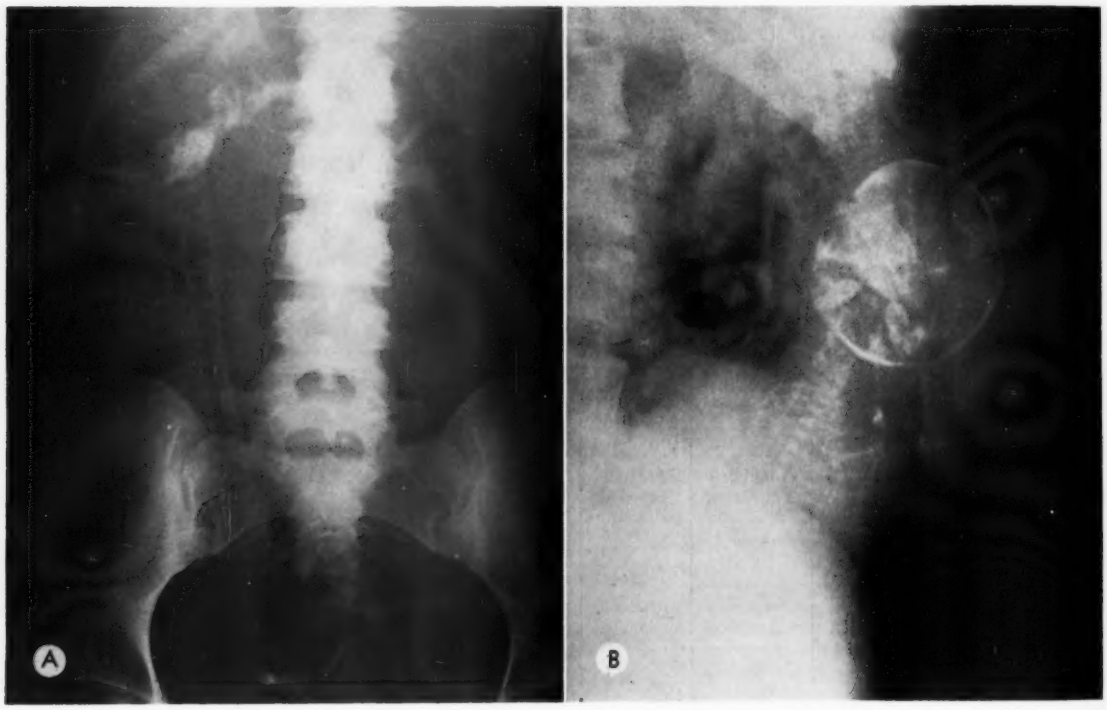

FIG. 4. Case 1. (*A* and *B*) The mother was a twenty-three year old white female, para II. The first baby, jaundiced at birth, is well at three years of age. During the second pregnancy, the patient developed signs of toxemia. Roentgenograms revealed a dead fetus, absence of a fetal fat line and elevated ribs of the fetus. The blood of the father was Rh positive; the blood of the mother was Rh negative and the anti Rh factor was present. Cesarean section revealed a dead fetus with fetal hydrops.

Fig. 5. Case 2. (*A* and *B*) The mother was a thirty-five year old white female, para IV. She had 3 norma pregnancies in close succession. The present pregnancy was normal up to thirty-eight weeks, when fetal movements and heart sounds were absent. Two days later profuse vaginal bleeding occurred. Roentgen examination for placenta previa revealed signs of fetal hydrops. Four days later a macerated dead fetus with fetal hydrops was delivered. The mother's blood was Rh negative; it had been Rh positive during the 3 previous pregnancies.

and increased density of soft parts. It is so striking in the scalp that a definite corona is seen surrounding the skull." They also speak of it as a "dark corona." A dark shadow could result only from tissues of decreased roentgenographic density similar to fat. Javert,[7] on the other hand, illustrates the halo sign in what appears to be a retouched reproduction in which the edematous scalp casts a shadow that is lighter than the surrounding soft tissues. The fact that such prominent proponents of the halo sign present it in opposite densities is confusing, to say the least. Postnatal roentgenograms reveal a thickened edematous scalp which casts a shadow of the same density as the other edematous soft tissues. That this "halo" is said to be present only in vertex presentations is also difficult to rationalize. We have observed on roentgenograms of many normal obstetrical cases with vertex presentation the shadows of the soft tissue planes of a partially filled and compressed maternal bladder cause an appearance strikingly similar to a "halo." McClure Browne[9] presents illustrations of 2 normal cases in which shadows about the head were interpreted as the halo sign. One of these is typical of compression of the maternal bladder by the presenting fetal head; the other appears to be the double bone shadow of the vertex due, I believe, to overlapping shadows of the parietal bones. We are not convinced that the halo sign is of diagnostic value. The mechanism of its production is not clear. Illustrations of it in the literature are confusing. It was not observed in any of our cases.

The increased bone density of the fetus likewise was not a striking feature in the prenatal roentgenograms in our series. Only in Case 3 was it of diagnostic significance. It was probably present in other cases but masked by the increased density

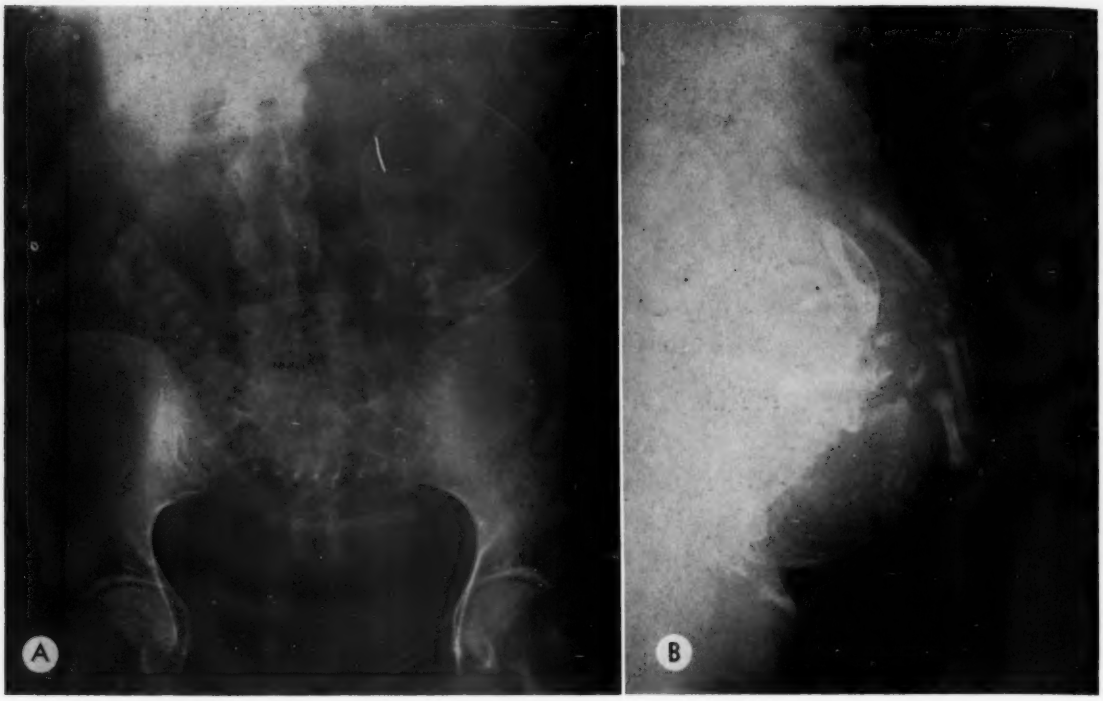

FIG. 6. Case 3. (*A* and *B*) The mother was a thirty-one year old white female, para III. She was known to have an Rh negative factor and had lost 2 previous pregnancies. During this pregnancy, no fetal heart sounds were heard at eight months. Roentgenograms revealed a dead fetus in a transverse lie with signs of fetal hydrops. The patient has since had a normal full term baby with no trouble whatsoever.

of the soft parts. Unfortunately, we do not have postnatal roentgenograms for proper evaluation of this feature. When increased bone density is observed on prenatal roentgenograms, in the absence of characteristic changes of fetal hydrops, it should arouse suspicion of the presence of one of the milder forms of erythroblastosis fetalis. In

FIG. 7. Case 4. The mother was a thirty-six year old white female, para V. In 1949 a pregnancy resulted in hydramnios, fetal anomalies, and stillbirth. In 1951 the patient delivered an erythroblastotic baby at full term. Because of the mother's Rh negative blood, neonatal anemia and enlargement of the liver, replacement transfusion was done. This child is living and well at six years. In 1953 a full term living baby was delivered. Replacement transfusion was performed but the indications are not recorded in the history. In 1955 the patient delivered a three week premature baby. Neonatal death occurred as a result of Rh sensitization. This pregnancy was of seven months' duration. Hydramnios had been noted to progress during the past two months. The fetal movements were active. The patient experienced vaginal bleeding which lasted for four days and a roentgenogram revealed evidence of fetal hydrops. Five days later a hydropic infant was delivered which lived only twenty-five minutes (see Fig. 1, *A–C*).

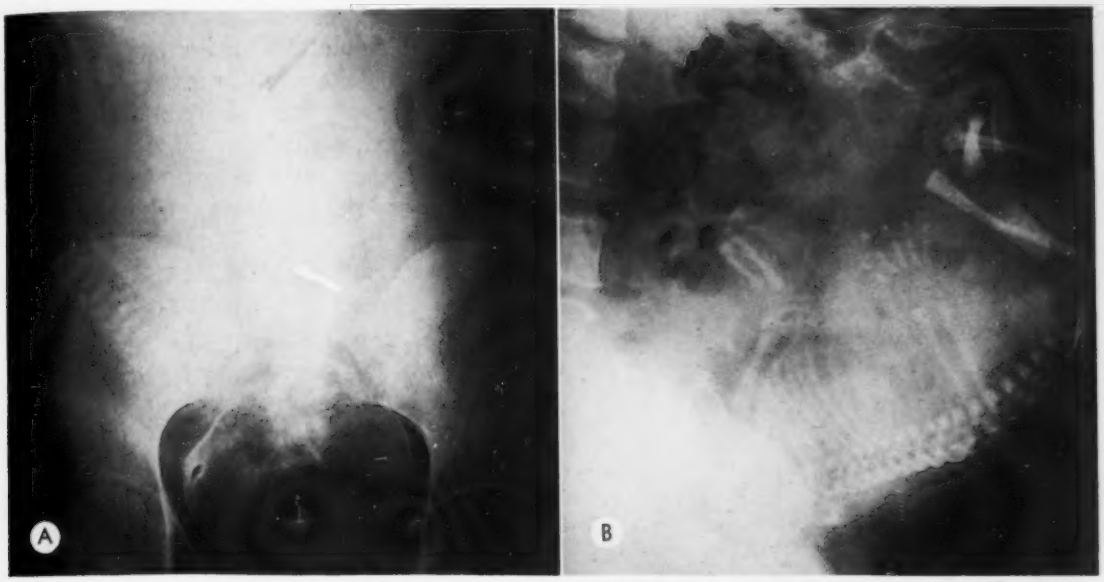

FIG. 8. Case 5. (*A* and *B*) The mother was a thirty-three year old white female, para III. In 1949 she delivered a normal child at term. In 1952 she also delivered an apparently normal child at term who, however, developed jaundice and facial edema the following day. The liver became enlarged and the general condition worsened. The child was found to have erythroblastosis due to a rare blood type, anti C (Fisher nomenclature), and developed cerebral palsy. The patient was admitted during this pregnancy at thirty-four weeks with hydramnios and painless bleeding. Roentgenograms made to determine the placental site or fetal anomaly were diagnostic of fetal hydrops. Cesarean section revealed a vigorous female child with severe fetal hydrops. The fetal weight was 2,730 gm., one quarter of which was estimated as due to edema. The liver and spleen were enlarged. Immediate transfusion with settled blood (Rh positive, Rh 1 homozygous) was given and 140 cc. of ascitic fluid was removed. A second exchange transfusion was performed when she was six and one-half hours old, a third on the third day and one when she was four days old. The child responded and is now well and flourishing.

postnatal studies this finding may be rewarding in making the diagnosis of questionable cases of fetal anemia or jaundice.

DISCUSSION

Erythroblastosis fetalis is a hemolytic clinico-pathologic syndrome of offspring, resulting from conception between an Rh negative woman and an Rh positive man. Fetal hydrops, the most severe form of this condition, is said to occur once in 2,000 deliveries. It is characterized by marked generalized edema of soft parts, associated with accumulation of fluid in the pericardial, pleural and peritoneal cavities, with enlargement of the heart, liver and spleen. The placenta is enlarged, thickened and edematous.

Due to advances in the care of premature infants and the spectacular results of prompt and repeated replacement blood transfusions, this condition is no longer a hopeless one. Early diagnosis and prompt therapy are essential. Roentgen studies are indicated whenever there is a clinical suspicion of hydramnios and in all pregnant women who are known to be Rh negative or who have previously had an erythroblastotic child.

The two best known diagnostic signs, the Buddha posture and the halo sign, have been unsatisfactory in the experience of many observers.

SUMMARY

Six cases of fetal hydrops correctly diagnosed by roentgenograms of the gravid abdomen are reported. The diagnostic features are based on both direct and indirect evidence of the pathologic changes:

1. Obliteration of the fetal fat line, due to subcutaneous edema.

FIG. 9. Case 6. The mother was a nineteen year old white female, para II. She was a known Rh negative who fifteen months previously delivered a full term fetus with fetal hydrops which lived only a few hours. A roentgenogram was made at thirty-four weeks to determine whether signs of erythroblastosis were present. There was no clinical suspicion of hydramnios, no toxemia, and no bleeding. The roentgenogram revealed findings typical of fetal hydrops and a cesarean section was performed. A markedly hydropic baby with an enlarged placenta was delivered and immediate replacement transfusion was given; however, the baby lived only two hours.

2. Displacement of the fetus an unusual distance from one side of the uterus, due to enlargement of the fetal abdomen and the placenta.

3. Elevation of the ribs, due to the enlarged heart and distended abdomen.

4. Peculiar posture of the arms and legs, due to soft tissue edema.

5. Intrauterine fetal death is a frequent finding.

In our experience the "halo" sign was not observed.

Chronologic review of our 6 cases gives us encouragement. The first 3 cases were dead at the time of the roentgen examination. The last 3 were delivered alive; one was salvaged, 2 died within short periods. It is our hope that this improvement is at least in part the result of the efforts of our clinico-roentgenologic teamwork and that our results can be projected to still more favorable levels in the future.

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A NEW METHOD OF FETAL WEIGHT DETERMINATION*

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THE existing methods of fetal weight determination have proved unsatisfactory at our Institution. It was felt that a more accurate method would have to be devised by which to ascertain the maturity of an infant before elective cesarean section or induction of labor is undertaken. The literature reveals approximately 5 per cent fetal mortality in elective cesarean sections due to prematurity.[1,3,6,9] This is a report of a new method of fetal weight determination which approaches satisfactory accuracy and is useful in cases when the obstetrician is not certain if the infant is mature enough to survive cesarean section or the induction of labor. Multiple measurements are used which when averaged together result in greater accuracy because of what we call the "equalizing factor."

EXISTING METHODS

The existing methods are based mostly on one measurement of the fetus. Following are the commonly used ones. The method of identifying the proximal tibial epiphysis which calcifies at the 39th or 40th week has been satisfactory if one can visualize it on the roentgenograms.[2] If the fetus is not of 39 or 40 weeks of gestation, the stage of maturity cannot be determined.

The distal femoral epiphysis calcifies at 35 to 40 weeks and again the same problem exists as in that of the proximal tibial epiphysis. Previous studies show that at 35 weeks the average fetus is 5 pounds and, therefore, by visualization of the distal femoral epiphysis, we cannot say unequivocally that a fetus is completely mature since the weight at this stage of gestation will vary from 5 pounds and up.[2]

The use of biparietal skull measurements allows us to consider only two-thirds of the cases examined due to lack of proper intrauterine position of the fetus. The literature reveals that with biparietal diameter measurements, two-thirds of the cases had an error of 1 pound greater or 1 pound less than the actual weight. Only infants weighing 5 pounds or more were used.[7] This does not take care of the "critical" range of 4 pounds to 6 pounds which we define as "that weight below which the fetus is obviously immature by clinical and/or roentgen methods and above which it is obviously mature by either or both methods."

The measurement by head volume reveals that this method will allow an error of 8 ounces or less in 36 per cent of the cases and an error of 16 ounces or less in 60 per cent of the cases.[4] However, all of the cases described in the literature in which this method was used were 6 pounds and 13 ounces or over, and, therefore, did not represent those of the "critical" weight group.

Other methods employed are those of measurement of fetal length, occipitofrontal diameter of the skull[10] and clinical estimation by measuring the uterus.[8]

INDICATIONS FOR ROENTGENOGRAPHIC EXAMINATION FOR FETAL WEIGHT

It is generally agreed that the indiscriminate use of roentgenography for determining fetal weight is to be avoided. Roentgenographic examinations, however, are indicated in cases where (1) elective cesarean sections are contemplated for the following reasons: (a) a repeat cesarean section is considered and the obstetrician is not certain of the degree of maturity of the

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fetus; (b) the mother is diabetic; (c) Rh problems exist; (d) cephalopelvic disproportion with a breech presentation is noted and, therefore, the patient cannot be given a trial of labor; (e) there is toxemia of pregnancy, and (2) the obstetrician may wish to induce labor and does not know the degree of maturity of the fetus.

RADIATION EXPOSURE

In order to reduce radiation to the maternal gonads, fetal gonads and to the entire body of the fetus to the least amount within practical limits, high speed screens with high speed film are recommended. A cone is used to collimate the roentgen-ray beam, and the beam is filtered with 2 mm. of aluminum which, in addition to approximately 0.5 mm. of aluminum inherent filtration, results in a total of 2.5 mm. of aluminum filtration. Webster and Merrill show that although the output varies among roentgenographic units, the anteroposterior projection results in an average of 250 mr to the maternal gonads and the lateral projection results in 280 mr to the gonads. The average total dose for the examination is 530 mr to the maternal gonads. There have been no studies of radiation received by the fetus itself and, therefore, it must be assumed that the dosage is slightly above that received by the maternal gonads in the anteroposterior projections, since the fetus is closer to the roentgen-ray tube. In the lateral projection there is probably very little difference. These figures are obtained with a 200 milliampere unit. A dose of 500 to 550 mr to the fetus and maternal gonads should not contraindicate an examination which may increase the survival rate of infants delivered by cesarean section.

TECHNIQUE

The success of our method depends upon satisfactory roentgenograms so that the landmarks may be accurately identified. Two roentgenograms are taken, one in the anteroposterior and one in the lateral projection. Wire abdominal markers are taped across the anterior portion of the abdomen for the lateral view and across the two lateral margins of the abdomen for the anteroposterior view. Solder wire has been used since it is very pliable and is radiopaque. This delineates the abdominal wall and, therefore, assists in obtaining measurements of the uterus with a greater degree of reliability. A constant tube film distance of 40 inches is used. In the graphs which are constructed, the average distortion produced by a 40 inch target film distance is considered, and, therefore, no correction factor need be used.

It is possible that logEtronic reproduction, by clearly delineating the fetal points of measurement, may increase the accuracy of the procedure; this method will be used in some of the future cases.

The radiologist should position the patient and check the roentgenograms before the patient is dismissed to ensure that they are adequate for measurement. The anteroposterior roentgenogram is taken first so that a determination of a cephalic or breech presentation may be made. If a breech presentation is present, the lateral roentgenogram should be taken with the fetal head closest to the film.

CONSTRUCTION OF GRAPHS

The results obtained in the examination of 50 patients were used to construct graphs relating the fetal weight to various measurements. Scatter graphs were made using known weights versus known measurements, where the fetus was delivered within a day or so following the taking of roentgenograms. When the patient did not deliver for a significant time interval after roentgenography, the weight of the fetus at the time of roentgenography was computed from a gestation versus weight table, which was constructed from Streeter's tables of 704 specimens.[5]

PROCEDURE

The measurements which are usually made are illustrated in Figure 1, *A* and *B*.

Step 1. Skull Measurement (Fig. 2). This

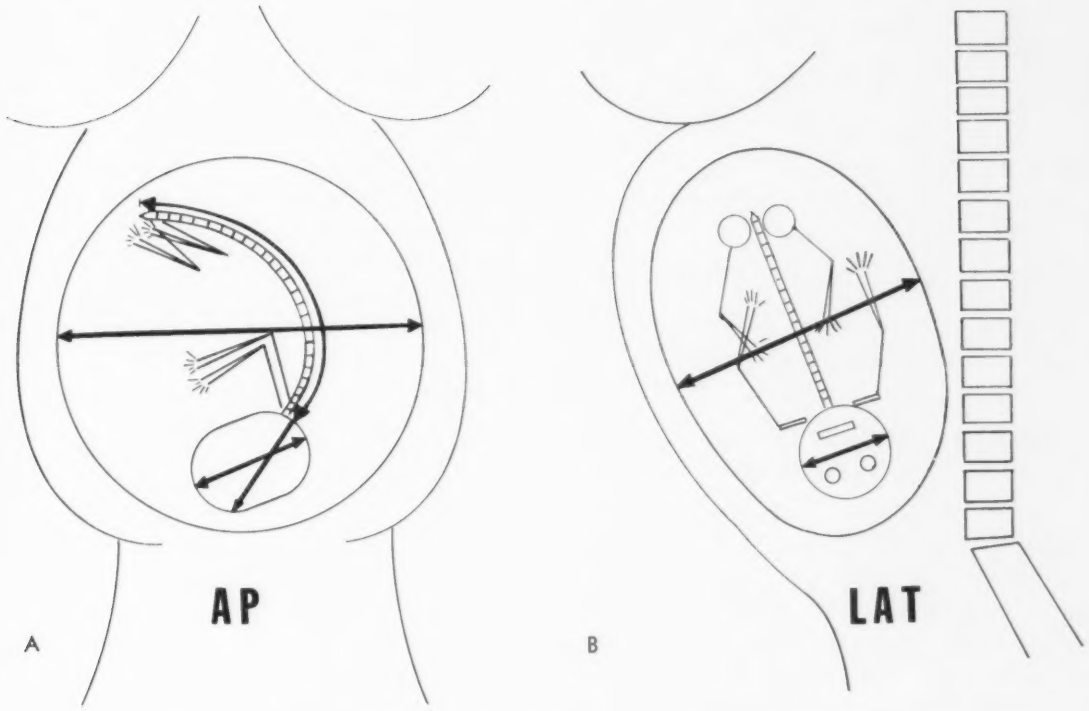

Fig. 1. (*A* and *B*) Schematic sketch showing measurements to be taken.

is found by (1) measuring the biparietal diameter of the skull; (2) measuring the occipitofrontal diameter of the skull, and (3) adding these two measurements together.

Generally, it is possible to obtain the biparietal measurement from the lateral roentgenogram and the occipitofrontal measurement from the anteroposterior roentgenogram. If only the biparietal diameter can be determined from both the anteroposterior and lateral roentgenogram, we have found that by adding 20 per cent to the biparietal diameter, we can arrive at the average occipitofrontal diameter. Conversely, if only the occipitofrontal measurement can be obtained, the biparietal measurement can be determined by subtracting 20 per cent from this measurement based on an average cephalic index of 8:10. This is the ratio of the broad diameter to the long diameter in the elliptically shaped skull and thus the sum of the biparietal and the occipitofrontal diameter cannot be in error by more than approximately 6 per cent. If the head is oblique in both projections, these two measurements are still added together.

(4) The fetal weight is taken from the skull versus weight graph.

Step II. Length Measurement (Fig. 3). This is found by (1) placing one point of a plastic flexible ruler at the coccyx and

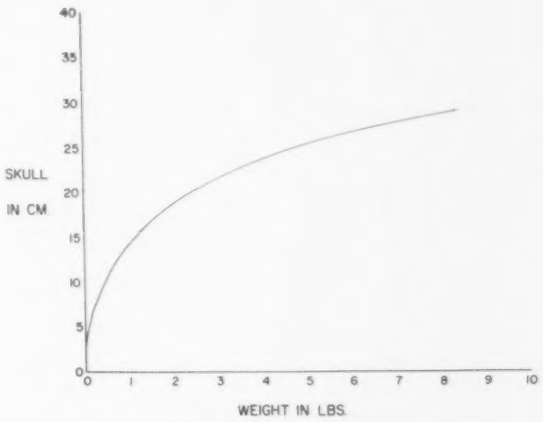

Fig. 2. Graph showing fetal weight versus skull measurements.

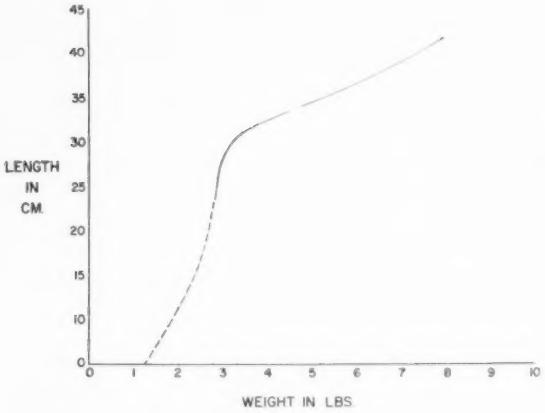

FIG. 3. Graph showing fetal weight versus length measurements.

measuring to the odontoid process along the contour of the spine; (2) drawing a line from this point to a point on the outer table of the skull which is at the greatest distance from the odontoid process; and (3) adding these two measurements together and thus obtaining the necessary figures for the total length versus weight graph. Here again, the graph was designed using the scatter graph method of known length versus known weight.

Step III. Uterus Measurement (Fig. 4). This is found by (1) measuring the greatest width of the uterus from the anteroposterior roentgenogram and the greatest width of the uterus from the lateral roentgenogram; and (2) adding these two measurements and then plotting them on the uterus measurements versus weight graph.

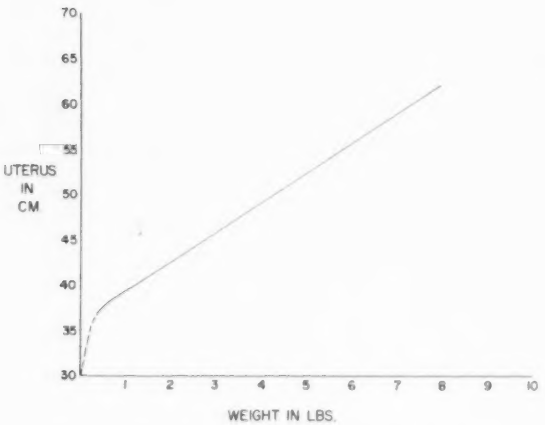

FIG. 4. Graph showing fetal weight versus uterus measurements.

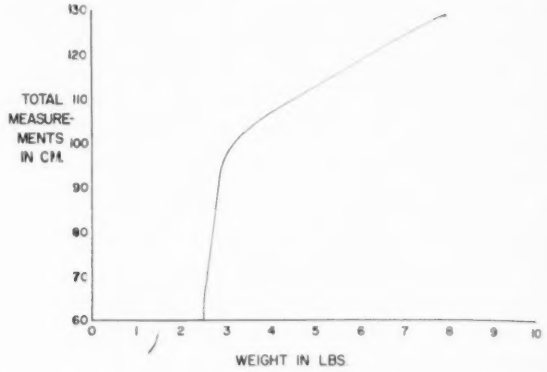

FIG. 5. Graph showing fetal weight versus total measurements.

Step IV. Totaling of Measurements (Fig. 5). This is done by (1) adding the measurements of the skull, length, and uterus; and (2) by plotting the sum on the total measurements versus weight graph.

Step V. Averaging. The weights obtained from the skull, length, uterus, and sum graphs are then totaled, and the average is found. This is the average or estimated weight of the fetus on the day of roentgenography.

It will be noted that the weights computed separately from the skull, length and uterus measurements may vary but the equalizing factor of the average weight results in the true weight.

Step VI. Gestation Determination (Fig. 6). This is found (1) after the estimated weight of the fetus has been determined. The expected weight increase may be obtained by using the gestation versus weight graph; then (2) the weight of the fetus at the time of roentgenography is recorded on the gestation weight graph. From the graph the number of weeks necessary for the desired increase in the weight of the fetus can be read.

UNUSUAL FETAL POSITIONS

Breech Presentation. Measurements are made in the same manner as in cases of cephalic presentation. The only change is

that the lateral roentgenogram is taken so that the head of the fetus is closest to the film. This can easily be determined after viewing the anteroposterior roentgenogram.

Transverse Presentation. After viewing the anteroposterior roentgenogram, the lateral roentgenogram is taken so that the head of the fetus is closest to the cassette. The skull and length measurements are determined in the same manner as in case of cephalic presentation. The measurement of the uterus from the anteroposterior roentgenogram is obtained in a cephalocaudal instead of the transverse dimension. On the lateral roentgenogram the measurement is taken through the greatest width of the uterus. All of the computations are then made in the same manner as for cephalic presentation.

Twin Pregnancy. Measurements are taken of only one of the intrauterine fetuses since twins are approximately of the same weight. The skull and length measurements are determined as in a single fetus. The uterus measurement is taken through the greatest width on both the anteroposterior and lateral roentgenogram. Seventy-five per cent of the total of the two measurements is used in computation since only the weight of one of the intrauterine fetuses is to be determined.

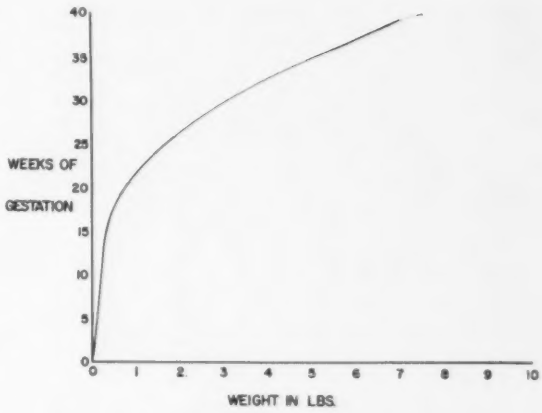

Fig. 6. Graph showing fetal weight versus weeks of gestation.

REPORT OF CASES

Case 1. M.J.A. This twenty-two year old pregnant Negro female (Fig. 7, *A* and *B*), who had a previous cesarean section, entered Milwaukee County Hospital with an unreliable

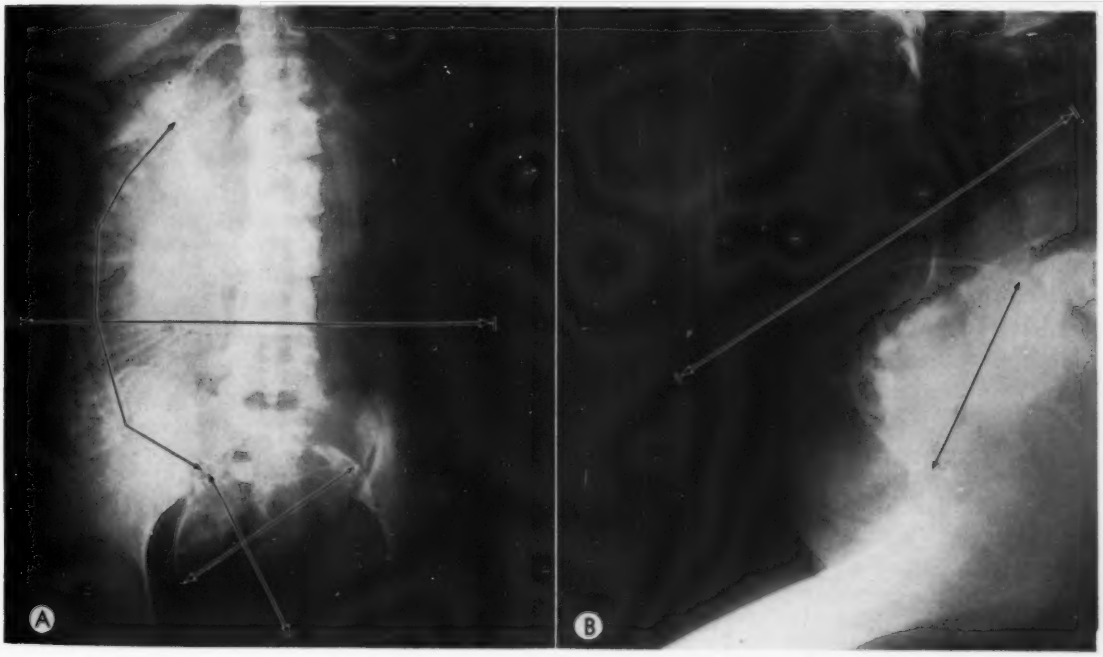

Fig. 7. (*A* and *B*) Case 1.

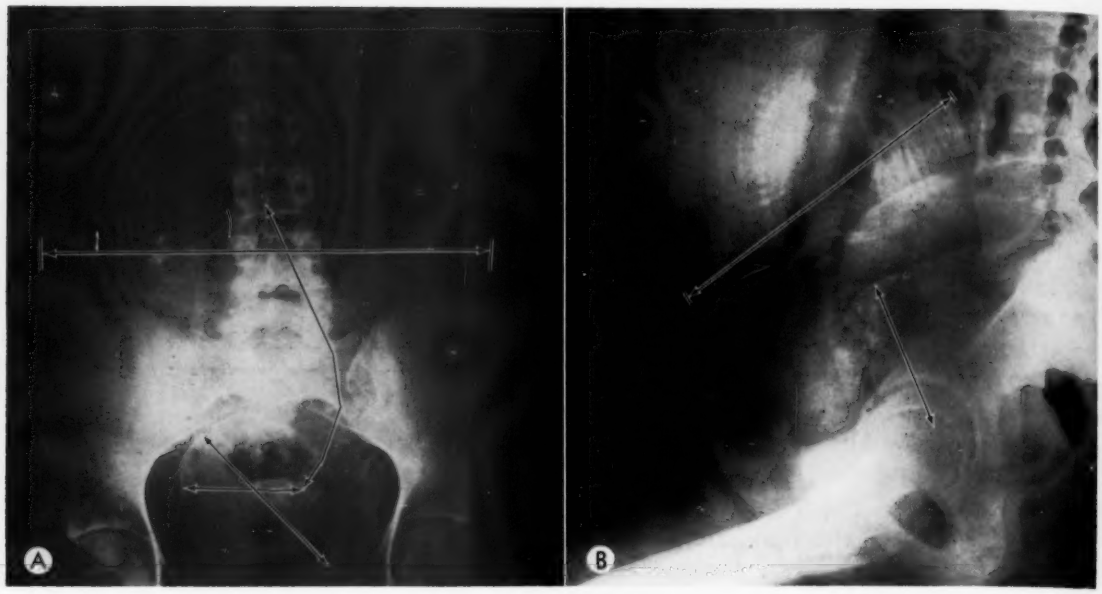

FIG. 8. (*A* and *B*) Case II.

menstrual history. The following statistical data were determined: skull—24.5 cm., 5 pounds; length—37.5 cm., 6 pounds 8 ounces; uterus—52.5 cm., 5 pounds; total—114.5 cm., 5 pounds 9 ounces; average weight—5 pounds 8 ounces; duration of gestation—36 weeks; time interval between roentgenography and birth—2 weeks; actual birth weight—6 pounds 3 ounces; estimated birth weight—6 pounds 8 ounces; error—5/101 = +5 per cent.

Comment. The average or estimated weight at the time of roentgenography was 5 pounds 8 ounces, which was approximately at 36 weeks of gestation. We suggested that an interval of two weeks should elapse before a cesarean section be done since our weight versus gestation graph revealed that at that time the fetus would weigh 6 pounds 8 ounces. This was done, and the actual birth weight was 6 pounds 3 ounces. By using this method premature birth was prevented.

CASE II. T.R. This twenty-eight year old white female (Fig. 8, *A* and *B*) entered the hospital for reasons unrelated to her pregnancy. Here again, the actual menstrual history was completely unreliable and roentgenograms were taken for future reference. The following statistical data were determined: skull—19.4 cm., 2 pounds 6 ounces; length—28 cm., 3 pounds; uterus—41.5 cm., 1 pound 12 ounces; total—88.9 cm., 2 pounds 9 ounces; average weight—2 pounds 7 ounces; duration of gestation—28 weeks; time interval between roentgenography and birth—11½ weeks; actual birth weight—7 pounds 6½ ounces; estimated birth weight—7 pounds 8 ounces; error—1.5/118.5 = +1 per cent.

Comment. This patient had a normal uneventful delivery. Nevertheless, by our method we were able to predict within 1 per cent the birth weight of the baby.

CASE III. This twenty-eight year old white female (Fig. 9, *A* and *B*) with an unreliable menstrual history entered the hospital for evaluation. The following statistical data were determined: skull—24.8 cm., 5 pounds 2 ounces; length—39 cm., 7 pounds; uterus—61.2 cm., 7 pounds 3 ounces; total—125 cm., 7 pounds 10 ounces; average weight—6 pounds 12 ounces; duration of gestation—38½ weeks; time interval between roentgenography and birth date—11 days; actual birth weight—7 pounds 6 ounces; estimated birth weight—7 pounds 8 ounces; error—2/118 = 2 per cent.

RESULTS

The degree of accuracy in a series of 179 cases is graphically illustrated in Figure 10.

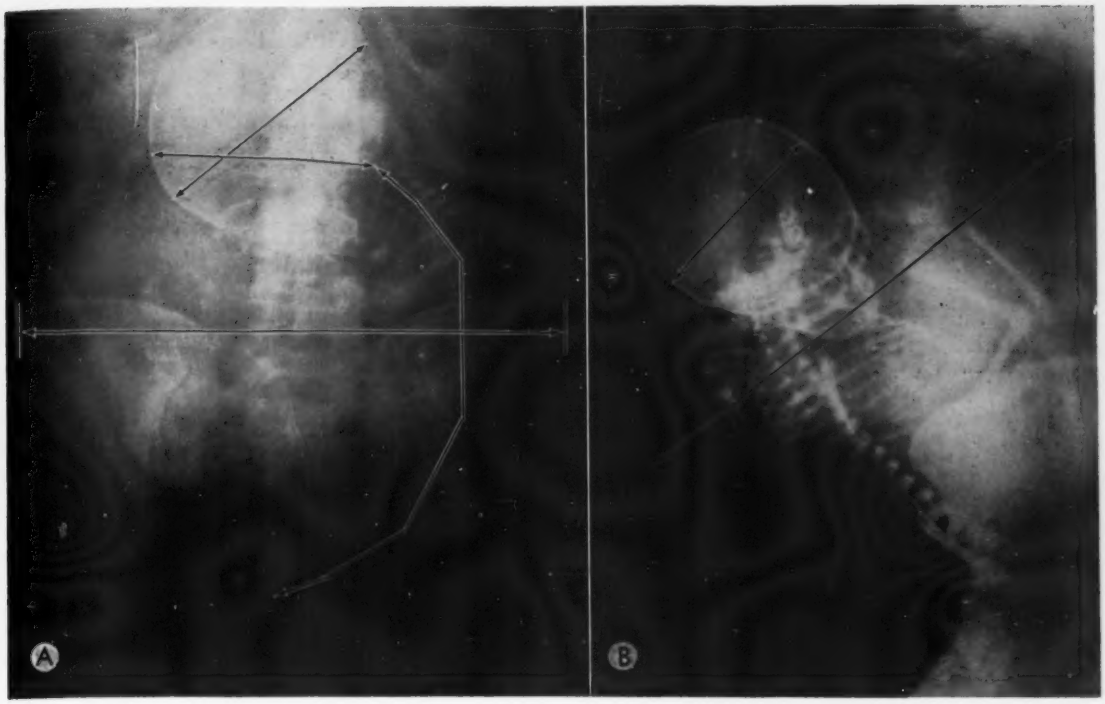

Fig. 9. (*A* and *B*) Case III.

SUMMARY

1. A report of a new method of fetal weight determination has been presented.
2. It is believed that its degree of accuracy is superior to that of other existing methods.
3. The ability to project the weight at birth is possible with this method.

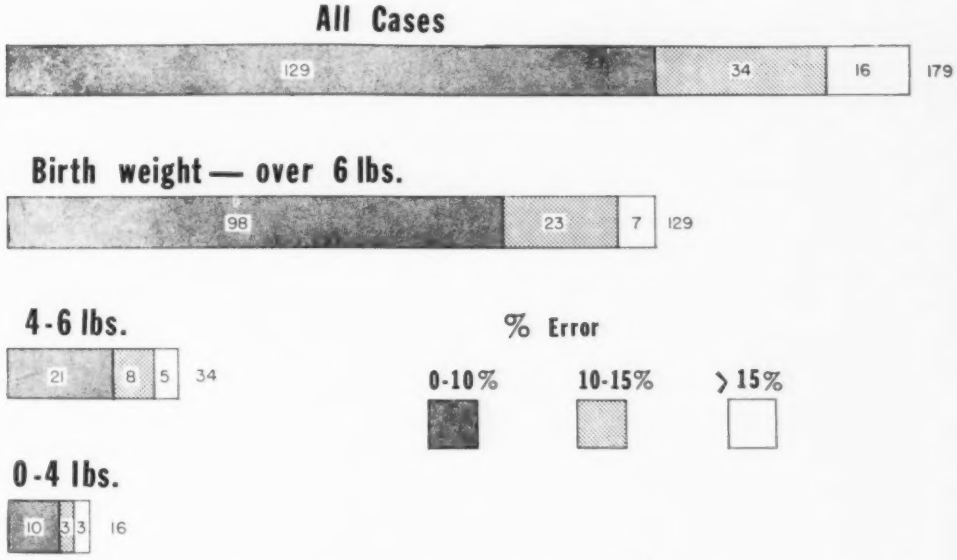

Fig. 10. Diagram showing the birth weight error.

4. Radiation exposure of the maternal gonads and fetus should not contraindicate an examination which may save the lives of 5 per cent of babies who are delivered by elective cesarean section.

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The authors wish to thank Dr. John R. Amberg, Chief of Radiology, John A. Lind and Calvin Williams, radiology residents, for their help in making this report possible.

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PREMATURE UNILATERAL SYNOSTOSIS OF THE CORONAL SUTURE*

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PREMATURE, unilateral, coronal synostosis (hereinafter referred to as unilateral coronostenosis) is a congenital abnormality of the skull with a distinctive combination of roentgenographic features. Failure to distinguish this entity from certain other diseases that affect the configuration of the skull may lead to unnecessary diagnostic procedures and to delayed or inappropriate treatment. McLaurin and Matson[12] advocate the earliest possible treatment for the prevention of exophthalmos, visual loss, cosmetic deformities and perhaps brain damage.

Since the most important findings necessary for early diagnosis are the roentgenographic signs, the radiologist has the responsibility of establishing or confirming the diagnosis. Because it is uncommon, this condition is likely to present a problem in roentgenologic interpretation. Case presentations and discussion of this form of craniostenosis, with emphasis on clinical and roentgenologic diagnosis, should make immediate recognition possible.

FIG. 1. Case 1. A one month old white female with right coronal synostosis. There is flattening of the right frontoparietal region, right sided exophthalmos, and minimal facial asymmetry.

REPORT OF CASES

CASE 1. T.C., a white female infant, was brought back to the physician who delivered her for a routine examination at the age of one month. At this time, the doctor noticed a slight exophthalmos of the right eye, flattening of the right frontal area of the skull, and minimal asymmetry of the face (Fig. 1). There were no other positive findings; development was normal and the neurologic examination revealed no abnormalities.

Roentgenograms of the skull demonstrated narrowing of the right coronal suture with fusion of its inferior portion (Fig. 2, *A* and *B*); this was more readily apparent on the roentgenograms made for the optic foramen (Fig. 3, *A* and *B*) which also showed narrowing of the sphenofrontal, sphenoparietal, squamosal, and sphenosquamosal sutures. The Water's projection (Fig. 4, *A* and *B*) revealed an elliptical shape to the enlarged right orbit, elevation of the right lesser sphenoid wing, slight flattening of the right parietal area, and slanting of the nasal septum with its cephalad end pointing to this same side. In the Towne view (Fig. 5, *A* and *B*), flattening of the parietal bone was more evident posteriorly and was associated with displacement of the posterior sagittal suture and lambda to the right. In addition, there was depression of the right petrous ridge and deepen-

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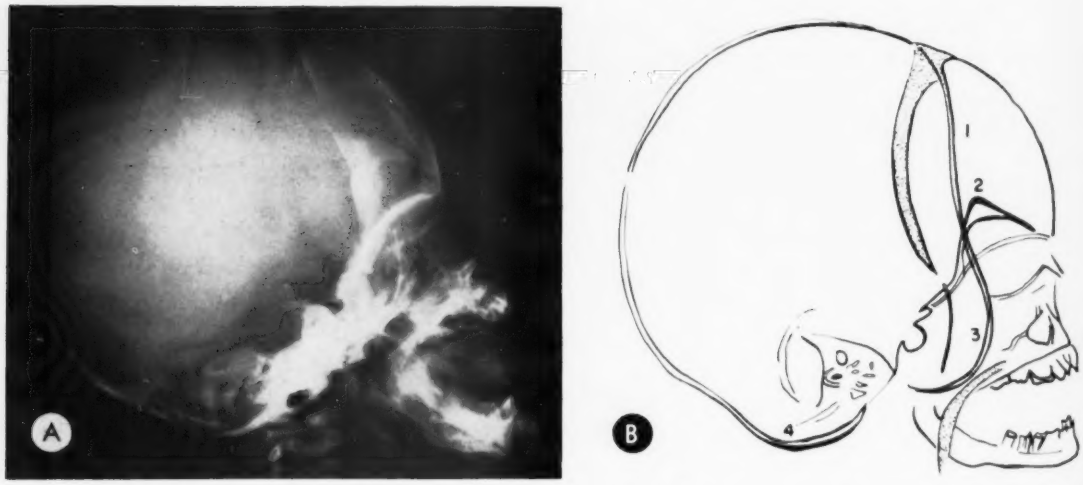

FIG. 2. Case 1. (*A* and *B*) Roentgenogram and its tracing showing narrowed right coronal suture (1); elevated right orbit (2); enlarged middle (3) and posterior (4) fossae. The right anterior fossa is shortened.

ing of the right middle and posterior fossa. Shortening of the anterior fossa with forward displacement of the anterior margin of the middle fossa was seen on the lateral roentgenogram (Fig. 2, *A* and *B*). Although the skull appeared to have an increased height, measurements were within the upper limits of normal.[5] There was no asymmetry in thickness of the calvarium and no increase in convolutional markings.

Corrective surgery was performed for right coronostenosis in the following manner: a small-nosed rongeur was used to make a false suture behind the right coronal suture. Polyethylene sheeting was placed between the cut edges and held in place by three sutures. The postsurgical course was uneventful. The infant was lost to follow-up two months later before postsurgical roentgenograms were made.

CASE II. M.M.L., a two and one-half year old female, had been in an automobile accident on January 5, 1960. She was never unconscious and did not exhibit any signs or symptoms indicative of brain injury, but the parents noted that the head was abnormal in appearance. The neurosurgeon to whom the child was referred reported discoloration around the right eye; a large and asymmetric head; high pitched percussion note; head measurements 2.5 cm. larger than normal for a child of this age; an unsatisfactory funduscopic examination, but there appeared to be some hemorrhage; equal and active deep reflexes; and normal muscle strengths in all extremities. It was not until later when he was asked to look carefully for this specific sign that the physician noted slight facial asymmetry. The child's development had been normal.

The skull roentgenograms revealed flattening and thinning of the parietal region, elliptical orbit with decreased depth, elevation of the lesser sphenoid wing, shortened anterior fossa, forward displacement of the greater sphenoid wing, enlargement of the middle and posterior fossae, and depression of the petrous ridge. All of these findings were asymmetrically located on the right (Fig. 6, 7 and 8). Mild obliquity of the nasal septum was also noted with its superior end pointing to the right and the posterior sagittal suture and lambda displaced considerably in the same direction. The length and breadth of the skull measured within limits of normal, but the height was increased. These roentgenograms were made elsewhere and the only lateral views available were some made at the time of pneumoencephalography. The coronal sutures were very poorly demonstrated and could not be evaluated. The radiologist considered tumor or hydrocephalus as well as unilateral, partial, and premature closure of the right coronal suture in the differential diagnosis. Pneumoencephalography was interpreted as normal.

Surgical correction for unilateral coronostenosis was performed by the neurosurgeon in the same manner as in the preceding case.

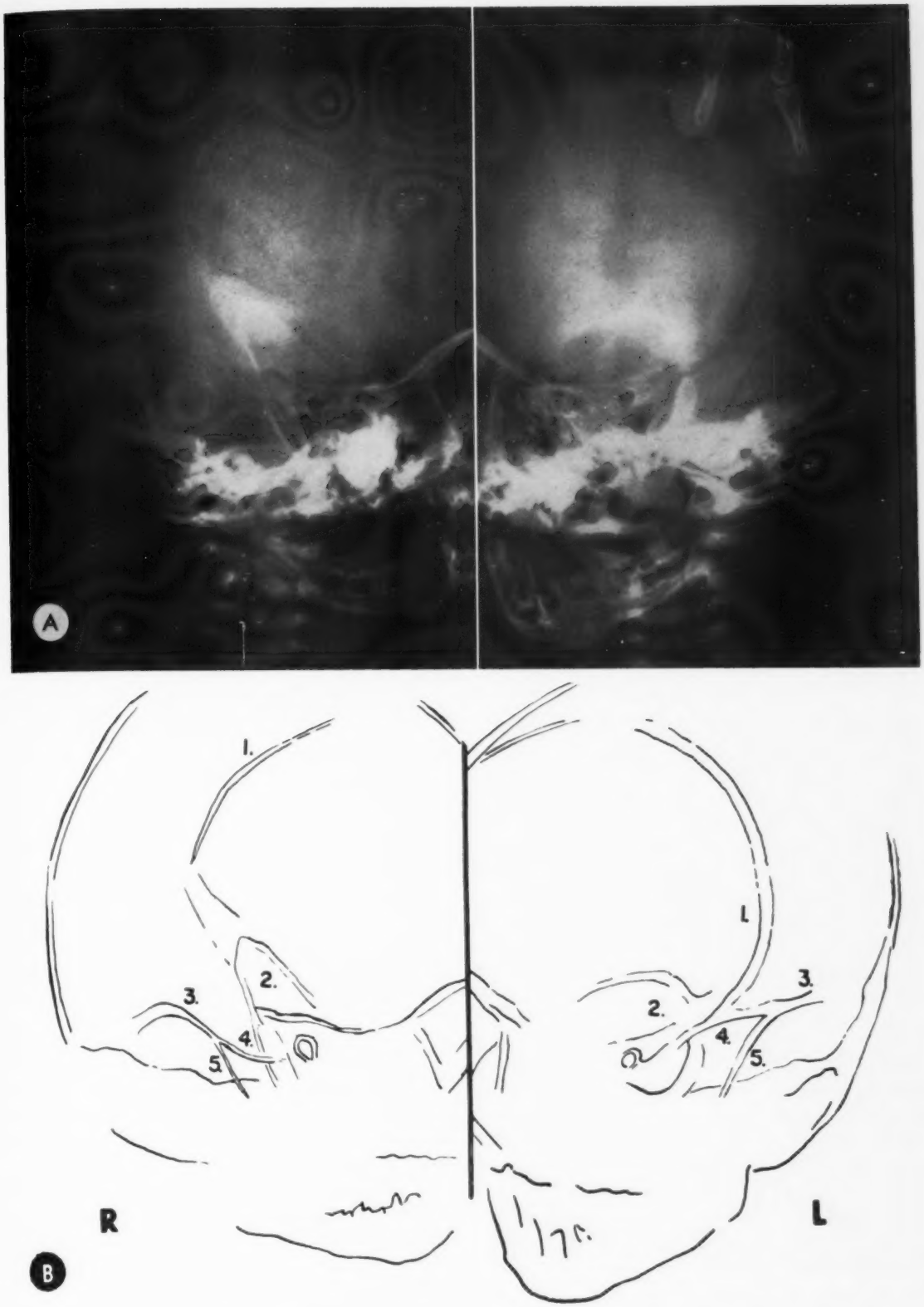

FIG. 3. Case 1. (*A* and *B*) The optic foramina are normal. The entire right coronal suture (1) on the right side is narrowed and synostosis is taking place in its inferior portion. There is also narrowing of the right squamosal (3), sphenoparietal and sphenofrontal (4), and sphenotemporal (5) sutures. The elliptical configuration of the right orbit (2) is well shown.

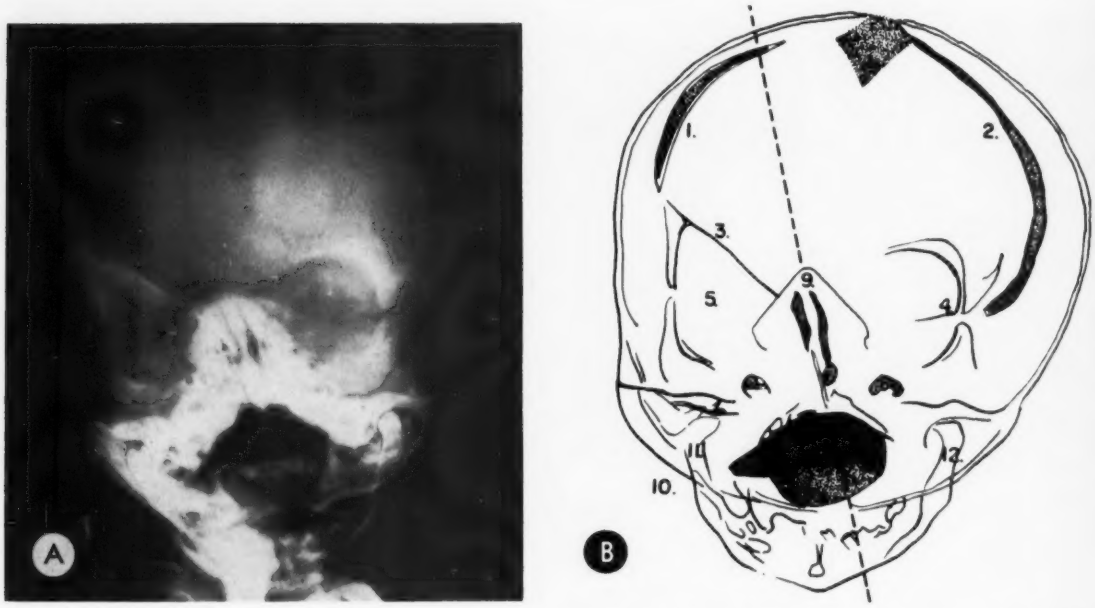

FIG. 4. Case 1. (*A* and *B*) Water's view showing elevation of the right sphenoid wing and sphenoid ridge (3), flattening of the right parietal area and obliquity of the nasal septum (9) with its superior end pointing to the side of the pathology. Right and left coronal suture (1 and 2); sphenoid wings (3 and 4); enlarged, elliptical right orbit (5); depressed right mandibular condyle (retouched) (11); and left mandibular condyle (12).

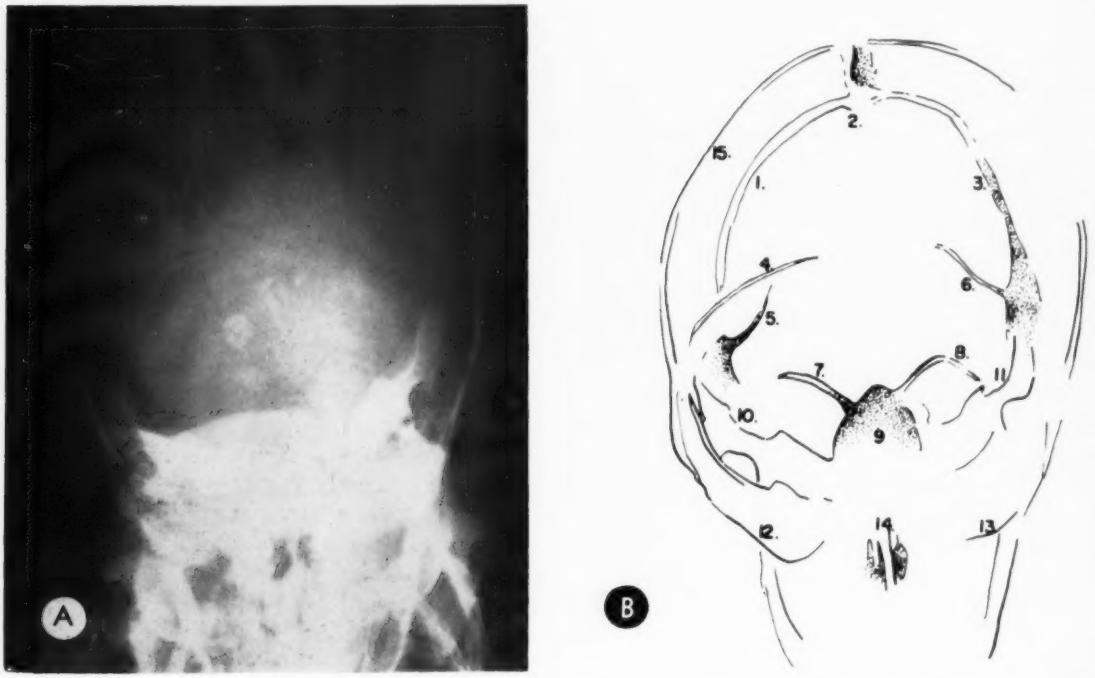

FIG. 5. Case 1. (*A* and *B*) Flattening of the right parietal region (15) is shown best in this Towne-Chamberlain projection as is the depression of the petrous ridge (10) on the same side. Lambdoidal sutures (1 and 3); lambda (2) displaced to right, mendosal sutures (5 and 6); narrowed right coronal suture (4); synchondrosis between ex-occipital and supra-occipital (7 and 8); depressed right petrous (10) and normal left petrous (11) ridges; depressed right middle (12) and normal left middle (13) fossae; and an oblique nasal septum (14) are also seen.

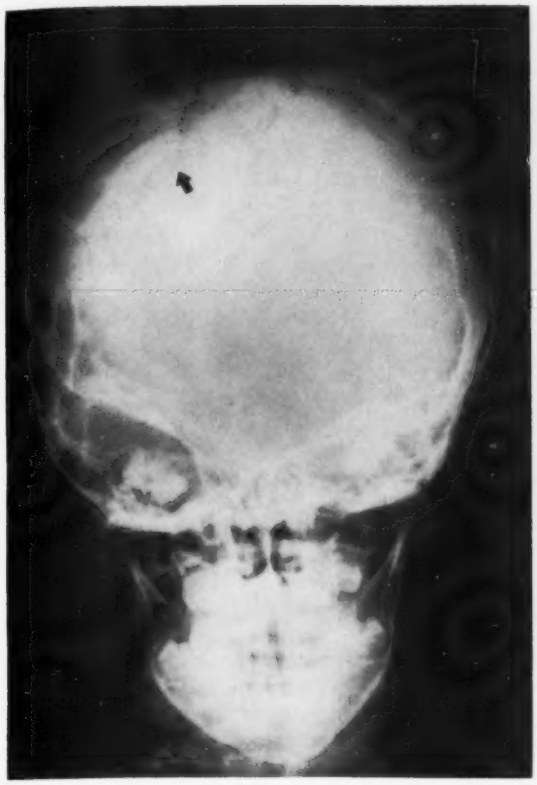

Fig. 6. Case II. Posteroanterior roentgenogram showing enlarged elliptical orbit, elevated sphenoid wings and deepening of the middle fossa, all on the right. There is also slight obliquity of the nasal septum and displacement of lambda to the right (arrow). Depression of the right middle fossa has resulted in the lower position of the right mandibular condyle (retouched).

Fig. 7. Case II. Roentgenogram of the sphenoid area showing the same findings as described in Figure 6. In addition, the double arrows point to the enlarged right posterior fossa. The single arrow points to lambda. This roentgenogram was made during pneumoencephalography.

Case III. S.B., a seven and one-half month old white female, was brought to the clinic because of irritability, particularly in the last three months, and also because of flattening of the right frontal region which has not been progressive. The mother had many roentgenograms and several operations for intestinal obstruction during the gestation period. The child was born prematurely but her development has been normal.

Physical examination revealed an irritable baby with flattening of the right frontal bone, elevation of the right orbital rim, elevation of the right eyebrow and slight facial asymmetry. There was also flattening of the right occipital region of moderate degree. The head size measured within normal limits. The motor reflex and sensory testing were normal. The ocular

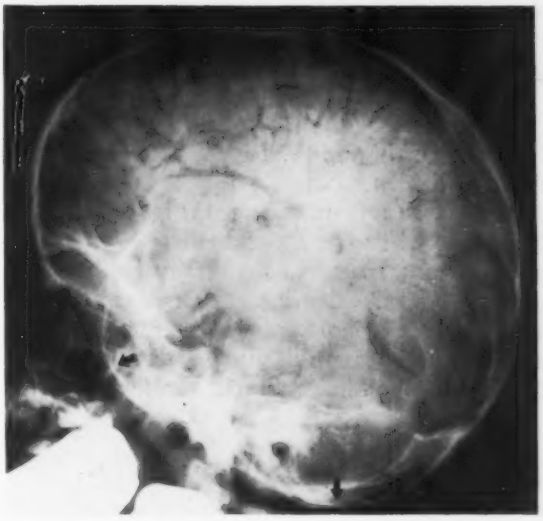

Fig. 8. Case II. Roentgenogram showing ventral bulging and apparent enlargement of the right middle fossa and enlargement of the right posterior fossa (arrows). This roentgenogram was made during pneumoencephalography.

FIG. 9. Case III. The obliquity of the nasal septum, displacement of lambda, elevated right sphenoid wing, and the elliptical right orbit are prominent findings. Asymmetry of the skull, depression of the right middle fossa, mandibular condyle, petrous ridge and posterior fossa are also shown.

FIG. 10. Case III. Asymmetry with flattening of the right parietal bone, depression of the right middle and posterior fossae and the right mandibular condyle (retouched) are shown best on this roentgenogram. The lambda is displaced to the right.

movements were of full range and the optic fundi were normal. The vision and hearing seemed to be normal. The electroencephalogram was normal.

Roentgenograms showed right, unilateral coronostenosis with associated findings as demonstrated in Figures 9, 10 and 11 and as indicated in Table 1.

A channel, 1.5 cm. wide, was made along the right coronal suture and extended down below the squamosal suture. No removal of orbital roof or lateral orbital wall was carried out. Polyethylene film was placed over the edges of this bone and heavy silk sutures were tied about the film through holes punched in the adjacent bone.

FIG. 11. Case III. Depression of the right posterior fossa appears to be the most prominent finding on the lateral roentgenogram. The deepening of the right middle fossa is less apparent and no bulging of its anterior margin is demonstrated.

GENERAL CLINICAL DISCUSSION

Unilateral coronostenosis is a congenital disease of unknown etiology with a familial tendency. The signs of synostosis are usually present at birth. Immediate postnatal recognition of the skull abnormality by the

TABLE I

FREQUENCY OF THE MOST IMPORTANT DIAGNOSTIC ROENTGENOGRAPHIC SIGNS OF UNILATERAL CORONOSTENOSIS IN 11 CASES (8 previously reported)

Roentgenographic Signs	Case I T.C.	Case II M.M.L.	Case III S.B.	Case IV[7]	Case V[19]	Case VI[12]	Case VII[16]	Case VIII[4]	Case IX[13]	Case X[9]	Case XI[18]
Orbit—Elliptical, Elevated and/or Enlarged	+	+	+	+	+	+	+	+	+	+	o
Lesser Sphenoid Wing—Elevated	+	+	+	+	+	+	+	+	+	+	o
Parietal Bone—Flattened	+	+	+	+	+	+	+	+	+	+	+
Parietal Bone—Thinned	−	+	−	−	−	−	−	−	+	+	−
Anterior Fossa—Shortened	+	+	o	+	o	o	o	o	o	+	o
Middle Fossa—Enlarged	+	+	+	o	o	o	o	o	o	o	o
Posterior Fossa—Deepened	+	+	+	+	+	+	+	+	+	o	+
Petrous Ridge—Depressed	+	−	+	+	+	−	+	+	+	+	+
Temporomandibular Fossa—Depressed	+	+	+	+	o	o	+	o	o	o	+
Nasal Septum—Obliqued	+	+	+	+	−(?)	+	+	o	+	o	+
Lambda—Deviated	+	+	+	+	+	o	+	−	o	−	o
Clinical Facial Asymmetry	+	+	+	+	+	+	o	o	o	o	o

Note: In most of the previously reported cases, only a single posteroanterior roentgenogram was available for study.
+ indicates that the sign was present.
− indicates that the sign was absent.
o indicates that the sign was not visualized well enough to evaluate.

clinician may be hampered by edema of the scalp and moulding of the skull secondary to the birth process but, as these effects subside, the asymmetry of the skull becomes more apparent. Consistently present is flattening of the frontal region; exophthalmos and facial asymmetry may be apparent clinically.

Failure to realize that unilateral exophthalmos may be associated with this disease can lead to confusion and erroneous diagnosis. Other causes of exophthalmos in this age group include brain tumor, subdural hematoma, arteriovenous aneurysm of the brain or orbit, orbital neoplasm, congenital cyst and hemangioma of the orbit, orbital hemorrhage, and defective development of the sphenoid bone. Flattening of the ipsilateral frontoparietal region would not be expected in these, however,

and exophthalmos associated with flattening therefore becomes a significant clinical sign for unilateral coronostenosis. The exophthalmos which occurs in defective development of the sphenoid bone is usually found to pulsate.[14] Pulsating exophthalmos also occurs in arteriovenous aneurysm of the brain, orbit and cavernous sinus, and a bruit is often associated in these cases.[17]

Asymmetric eye signs in unilateral coronostenosis are due to the deformity of the orbit on the involved side[11] and to premature fusion of the orbital bones.[12] Hyperopia results from shortening of the orbit and is sometimes associated with astigmatism; divergent strabismus is common[11] and optic atrophy may occur with blindness[13] due to bony pressure on the optic nerve.[19]

Asymmetric flattening of the skull may occur in other entities and is most often due to longstanding postural pressure by chronic resting of the head in one position during infancy; this is usually seen in defective infants who move their heads little and in infants with soft skulls.[4] The appearance of these infants may at times cause the clinician to think of plagiocephaly, but the history, clinical observations and roentgenographic findings should help to establish the correct diagnosis. Asymmetry of the skull also may occur with scoliosis and torticollis, which have been referred to as scoliosis capitis,[9] but this occurs later and should present no difficulty in differentiation. The asymmetry seen in hemiatrophy of the brain occurs later in infancy or childhood than that due to a craniostenosis, and the degree of asymmetry is less obvious. Nevertheless, where exophthalmos is absent, cerebral hemiatrophy must be a serious consideration. Subdural hematoma and brain tumor sometimes cause skull asymmetry but, in these cases, the asymmetry is due to bulging on the side of the pathology which can usually be suspected and localized by the neurologic signs. Unilateral coronostenosis, with the exception of eye signs, is not associated with abnormal neurologic findings.

A palpable ridge at the margins of the coronal suture and immobility of the adjacent frontal and parietal bones are additional clinical signs of coronostenosis; mental retardation is commonly found in bilateral coronostenosis but is infrequent in the unilateral form.[3,8] Congenital abnormalities are often found in association with coronostenosis[4,7,12,13,19] and include syndactylism, congenital heart disease, meningocele, cleft palate, micrognathia as the more common varieties. No associated congenital abnormalities were noted in the presented cases or mentioned in those cases of unilateral involvement reviewed in the literature. However, only 2 of the published cases gave summaries of the history and clinical findings.

Facial asymmetry may occur and, when present, varies from a "bashed in" appearance[6] to slight elongation of the face on the involved side. There are other causes of facial asymmetry, including progressive facial hemiatrophy (Romberg's syndrome).[2,10,15] This entity is not associated with skull asymmetry and it occurs later.

Treatment. Wide resection of the pericranium followed by linear craniectomy, producing channels 1.0 to 1.5 cm. wide and parallel to the prematurely fused suture, is the surgery of choice; the bone edges are encased in tantalum foil, acrylic polyethylene tubing, or polyethylene film,[1] the latter being the substance of choice at present. Anderson and Johnson[1] recommend application of Zenker's acetic fixative solution to the exposed dura mater to delay regeneration of bone. When fusion of the bones of the orbit has resulted in exophthalmos, resection of the roof and lateral orbital wall is advised in addition.[12] The squamosal suture should also be visualized and, if fusion has also occurred here, then subtemporal decompression or extension of the craniectomy posteriorly along the squamosal suture has been recommended.

The danger of surgery in proper hands is small relative to the risks of blindness and of psychologic effects secondary to the deformity.[19] A difference of opinion

exists regarding surgical intervention, however, and some[3,8] argue that prophylactic surgery is unnecessary unless progress roentgenograms show extension of the synostosis to involve other sutures or unless cerebral symptoms develop.

Prognosis. In the experience of those with large series of unilateral coronostenosis, this deformity is not accompanied by any brain disturbances.[8] However, not all the sutures undergo closure at the same time in craniostenosis, and subsequent development of premature synostosis in other sutures, particularly in unilateral coronostenosis, is especially likely.[8,19] Patients with unilateral coronostenosis must therefore be closely observed by periodic examinations since brain damage and mental retardation occur frequently when coronal synostosis is bilateral.

Surgical intervention can reduce exophthalmos and strabismus and can prevent blindness. Progressive cosmetic deformity is prevented by the surgery and, as skull growth continues, these deformities tend to correct themselves.

Following craniectomy, there is a tendency for the surgically formed sutures to close within four to eight months, necessitating reoperation in many.[8] Use of the polyethylene film to cover the bone edges has obviated reoperation in most cases but, occasionally, its use is ineffectual.[11] Anderson and Johnson[1] have found that use of polyethylene film delays closure of the surgical sutures for two years or more, and application of Zenker's acetic solution to the dura at the operative site was found to be "probably even more effective."

ROENTGENOLOGIC DISCUSSION

The roentgenologic signs of premature, unilateral coronostenosis include flattening of the frontoparietal and posterior parietal regions; narrowing of the coronal suture, sometimes with sclerosis; elevation of the ipsilateral lesser sphenoid wing and superior margin of the greater sphenoid wing; elliptical orbit enlarged in the coronal plane but diminished in depth on the involved side. The anterior fossa on the ipsilateral side is shallow and shortened and associated with enlargement and deepening of the middle and posterior fossae and depression of the petrous ridge. Displacement of the lambda to the involved side and obliquity of the nasal septum, directed superiorly toward the side of the involved suture, are prominent findings. Although the infant's features may show a marked asymmetry, true asymmetry of the facial bones is either uncommon or difficult to demonstrate roentgenographically. The clinical appearance most likely results from depression of the temporomandibular fossa second to depression of the floor of the middle fossa and consequently of the mandible on the involved side. Thinning of the affected area of the calvarium occurs occasionally. Increased convolutional markings on the same side may be seen in older patients in whom the process is of longer duration, but these are not ordinarily present in infants.

Roentgenograms of the 3 cases presented and of other cases of unilateral coronostenosis reproduced in the literature (Table 1) reveal that certain roentgenographic features (elliptically shaped orbit, elevation of the lesser sphenoid wing, flattening of the parietal region, shortening of the anterior fossa, and enlargement of the middle and posterior fossa) are present in all cases that could be analyzed for these signs. The obliqued nasal septum was found in all but 1 case. Displacement of lambda toward the involved side was a conspicuous finding in 2 cases reported here and in 4 of 6 published cases in which the lambda was demonstrable. The coronal suture was not visualized satisfactorily in 1 of our 3 cases, and the roentgenograms of cases reproduced in the literature usually included only anteroposterior or posteroanterior projections, views in which the coronal suture is not well demonstrated. Of course, when premature narrowing of one of the coronal sutures is shown, this is *prima facie* evidence of premature synostosis, but narrowing of the suture in the absence of marginal sclerosis may be difficult

to recognize or to demonstrate roentgenographically. Nevertheless, even prior to closure of the suture or in the absence of coronal suture visualization, the diagnosis of unilateral coronostenosis may be made with confidence by means of roentgenographic signs which are consistently present.

On being confronted with the skull roentgrams in a case of unilateral coronostenosis for the first time, the possibilities that may come to mind include cerebral hemiatrophy, chronic or recurring subdural hematomas, neurofibromatosis, a slowly growing brain tumor, space-occupying lesions of the orbit, developmental defects of the orbital wall,[14,16] postural asymmetry of the skull, and scoliosis capitis. Analysis of the roentgenograms in these diseases reveals that, although there are several features, including unilateral elevation of the sphenoid wings and asymmetry of the parietal area, which suggest coronostenosis, certain other findings are not consistent with this diagnosis.

On the involved side in chronic or relapsing subdural hematoma, subdural hygroma, and other large, *chronic, space-occupying lesions* of the brain, the skull asymmetry is due to bulging of the ipsilateral temporoparietal region instead of flattening. There may be unilateral bulging of the middle fossa anteriorly, and the sphenoid wings may be pushed up by the same process, but the orbital appearance typical of coronostenosis is absent. The petrous ridge may be elevated in chronic subdural hematoma (when chronic hemiatrophy develops secondarily) and depressed in large, slowly growing brain tumors. Bone destruction in the sella turcica or orbit may be present, especially in neurofibromatosis, and this helps to exclude coronostenosis. Obliquity of the nasal septum is much less marked and much less common in the space-occupying group and, when it occurs, the deviation is more often away from the lesion.

In unilateral coronostenosis as opposed to *cerebral hemiatrophy*, there is absence of asymmetric thickening of the calvarium (and sometimes there is thinning), the petrous ridge is not elevated (and is usually depressed instead), and elevation of the lesser sphenoid wing is much more marked. Shortening of the anterior fossa and diminished orbital depth are not features of cerebral hemiatrophy. Although premature synostosis of the coronal suture probably can occur as a result of hemiatrophy of the brain, it is a secondary process which is rare; the appearance suggesting synostosis in these cases is almost always due to narrowing and overlap of sutures instead.[7] Asymmetry of the facial bones on the same side may occasionally occur with unilateral coronostenosis but has not been described in hemiatrophy. Obliquity of the nasal septum, commonly found in unilateral coronostenosis, makes a considerably less frequent and much less pronounced appearance in cerebral hemiatrophy. These roentgenographic differences also apply to porencephalic cyst except that, in the latter, a local area of thinning or bulging of the calvarium adjacent to the cyst may be present.

Postural asymmetry of the skull and *scoliosis capitis* should present no difficulties in the differential diagnosis, particularly if the clinical history is known.

Congenital absence of the superior orbital wall can give an abnormal appearance to the bony orbit somewhat suggestive of unilateral coronostenosis but has certain features absent in the latter; a portion of the bony orbit is missing, the orbit does not have the typical elliptical appearance, there is always bulging of the temporal fossa, a temporal bone hiatus is present, and abnormality of the sella turcica, which is sometimes deep and sometimes wide and shallow, may be found.[14] Minor unilateral elevation of the lesser sphenoid wing has been noted to occur in *unilateral agenesis* of the eye; this may resemble coronostenosis but the involved orbit is small as opposed to the enlargement usually noted in coronostenosis, and the other signs of unilateral coronostenosis are missing.

Orbital tumors, including neurofibromatosis, and *orbital arteriovenous aneurysms* occasionally cause enlargement of the bony orbit and may cause elevation of the sphenoid wings but, in these, the orbital appearance of coronostenosis is absent, the optic foramen may be enlarged and there may be destruction of the bony orbit.

The typical elliptical shape of the bony orbit in coronostenosis, which Hope[6] likens to the appearance of women's modernistic eyeglasses, is formed by the elevation of the upper, outer corner of the orbit. The superior and lateral orbital margins are straightened and slanted superiorly and laterally; the orbital depth is decreased while the orbit, projected in posteroanterior or anteroposterior views, usually appears enlarged. This appearance was present in all cases of coronostenosis that could be analyzed and is a pathognomonic feature. It is not a finding of any other disease.

In most cases of unilateral coronostenosis, the nasal septum, although ordinarily straight, is seen to lie in oblique position with its superior end deflected towards the synostosis. A similar appearance may occur in any case of craniostenosis with asymmetry of the skull, as in microcephaly and oxycephaly when one coronal suture closes before the other. It is a seldom and minimal finding in cerebral hemiatrophy, porencephaly and the Sturge-Weber disease where the deviation is towards the lesion, and in chronic or relapsing subdural hematoma in which slight deflection of the septum is more often in the opposite direction from the side of the pathology. When marked, as in Case 1, obliquity of the nasal septum is found only in plagiocephaly.

Asymmetry of the face is clinically evident in most cases of unilateral coronostenosis and, although synostosis of the facial bones on the same side occasionally might explain this, depression of the ipsilateral temporomandibular fossa and consequent asymmetric displacement of the mandible is probably the far more frequent reason. That there are some instances of facial asymmetry secondary to true synostosis of the facial bones was suggested by the roentgenograms in Case x, Table 1. In some, the clinical asymmetry may be more apparent than real, an optical illusion due to the unilateral flattening in the frontal region.

Although both are found in unilateral coronostenosis, there is no evidence for any direct cause and effect relationship between septal deviation and facial bony synostosis. This tends to be confirmed by the absence of nasal septum obliquity in progressive facial hemiatrophy as seen in 3 cases reviewed in the literature.[2]

MECHANISM OF THE ANATOMIC CHANGES

The abnormalities of the skull which characterize unilateral coronostensosis may be explained on the basis of knowledge that growth of the bones of the skull occurs at the sutural margins and depends on the expanding effect of the growing brain without which the bone growth will cease.

When premature synostosis occurs at the coronal suture, there is cessation of growth of the parietal and frontal bones at right angles to this suture. Growth continues at uninvolved margins of these bones and other cranial bones apparently with a compensating increase. This results in flattening of the cranium in the frontal and posterior parietal regions of the involved side. The frontal flattening is the more pronounced. While the affected parietal and frontal bones are shortened, their opposite numbers are not, so that lambda and the posterior sagittal suture are displaced to the shorter side of the skull.

The elevation of the lesser sphenoid wing and the superior margin of the greater sphenoid wing and orbital roof is due to the same process. In addition, synostosis may occur at the squamous suture and its extensions, the sphenoparietal and the sphenofrontal sutures, so that the elevation of the lateral margin of the orbit and the sphenoid areas is accentuated.

The nasal septum articulates with the sphenoid bone and any alteration in growth

of the sphenoid must involve this bone. Displacement of the nasal septum towards the side of the synostosis would therefore be expected in conjunction with the deviation of the sphenoid.

The stimulus of the rapidly enlarging brain results in increased bone growth at the uninvolved sutures, and this effect is most pronounced at those sutures near the site of the coronostenosis. It represents a compensatory mechanism which explains the enlarged middle and posterior fossae, depression of the petrous ridge and the absence of significant brain damage.

Modeling due to osteoclastic and osteoblastic activity secondary to pressure exerted by the expanding brain could account for thinning of the affected bone.

Facial asymmetry is apparently the result of enlarging and deepening of the ipsilateral middle fossa which results in displacement inferiorly of the mandibular condyle on the involved side. True unilateral synostosis of the facial bones must be rare.

SUMMARY

CLINICAL SIGNS OF UNILATERAL CORONOSTENOSIS

1. Asymmetric flattening of the posterior parietal and frontoparietal areas.
2. Ridging at margins of involved coronal suture and immobility of adjacent skull bones.
3. Unilateral exophthalmos and divergent strabismus.
4. Asymmetry of the face.
5. Mental retardation in bilateral coronostenosis, but infrequently in unilateral involvement of the coronal suture.
6. Often associated other congenital abnormalities.
7. Appearance of clinical signs in first year of life.

ROENTGENOGRAPHIC SIGNS OF UNILATERAL CORONOSTENOSIS

1. Narrowing of the involved coronal sutures, sometimes with sclerosis.
2. Elliptical, shallow bony orbit, enlarged in the coronal plane, on the same side.
3. Elevation of the ipsilateral lesser sphenoid wing.
4. Flattening of the calvarium, and sometimes thinning, on the side of the synostosis.
5. Shortening of the anterior fossa of skull associated with enlargement of the middle and posterior fossa on the involved side.
6. Depression of petrous ridge on the ipsilateral side.
7. Obliquity of nasal septum directed superiorly toward the side of the involved coronal suture.
8. Deviation of lambda to the same side.
9. Asymmetric position of the mandible and, rarely, asymmetry of the facial bones.

DIFFERENTIAL DIAGNOSIS OF UNILATERAL CORONOSTENOSIS

A. Disease entities most difficult to exclude clinically (these all develop at a later age):

1. Cerebral hemiatrophy and porencephalic cysts.
2. Space-occupying brain lesions including subdural hematomas and brain tumors.
3. Space-occupying lesions of the orbit (tumors and aneurysms).
4. Defective development of the bony orbit.
5. Facial hemiatrophy (Romberg's syndrome).

B. Roentgenographic signs of unilateral coronostenosis as aids in differential diagnosis of these diseases:

1. *Elliptical orbit*, associated with flattening of the frontoparietal or posteroparietal region and elevation of the lesser sphenoid wing on the same side, rules out all other diseases.
2. *Flattening of the parietal bone*, when it occurs with ipsilateral lesser sphenoid wing elevation, excludes all other diseases except possibly cerebral hemiatrophy. In the presence of an elliptical orbit, cerebral hemiatrophy can also be ruled out.
3. *Marked obliquity of a straight nasal septum* is not seen in any other disease, al-

though mild degrees of obliquity sometimes occur in cerebral hemiatrophy and subdural hematoma.

4. *Enlarged middle fossa* permits, in addition to unilateral coronal synostosis, consideration only of space-occupying lesions of the brain (tumors, aneurysms, and chronic and relapsing subdural hematomas).

5. *Depression of the petrous ridge* excludes all other lesions except brain tumors and the rare case of huge aneurysm.

6. *Elevation of the lesser sphenoid wing* may occur in all the diseases listed above under "A" with the exception of progressive facial hemiatrophy.

7. *Facial asymmetry* (but not obliquity of nasal septum or asymmetry of skull) is found in progressive facial hemiatrophy.

8. *Displacement of lambda* in the degree evident in these cases of coronostenosis and in other forms of plagiocephaly is not seen in other conditions.

(Note: unilateral synostosis of the lambdoidal suture can give the same findings except for the elliptical orbit and elevated sphenoid wing.)

CONCLUSIONS

1. Three cases of premature, unilateral synostosis of the coronal suture have been presented along with an analysis of those roentgenograms reproduced in the literature, and this entity is discussed particularly from a standpoint of clinical and roentgenologic diagnosis.

2. When surgical treatment is indicated, early diagnosis is necessary to permit intervention before the complications of craniostenosis are permanently established.

3. Early recognition of this condition is a roentgenologic responsibility.

4. When exophthalmos occurs with frontoparietal and posterior parietal flattening, the clinical evidence is strongly suggestive of unilateral coronostenosis. Nevertheless, cerebral hemiatrophy can be differentiated with certainty only by roentgenographic examination.

5. Narrowing of the coronal suture, when present, is *prima facie* evidence of coronostenosis, but this may be absent early in the disease or difficult to demonstrate. However, an enlarged, elliptical orbit (as seen on posteroanterior and anteroposterior roentgenograms) is always present and is a pathognomonic sign. The correctness of the diagnosis may be confirmed by the other roentgenographic signs on the ipsilateral side, especially the following: (a) elevated sphenoid wing and (b) flattened parietal bone.

6. Obliquity of the nasal septum is a helpful adjunctive sign which, when of marked degree, has been found only in plagiocephaly. Out of 10 cases of coronostenosis that could be analyzed for this sign, it was present in 9.

7. Definite displacement of lambda to the involved side has not been noted in conditions other than plagiocephaly.

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Vol. 86, No. 3

SKULL CHANGES IN IRON DEFICIENCY ANEMIA SIMULATING CONGENITAL HEMOLYTIC ANEMIA*

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WIDENING of the diploic space and thinning of the outer table of the skull, originally described in children with chronic hemolytic anemia, were reported for the first time in a child without hemolytic anemia or red blood cell sickling by Feingold and Case[7] in 1933. A museum study of the skulls of ancient Peruvians, by these authors, revealed that the incidence of similar skull changes was far greater than the anticipated incidence of hemolytic disease. The relationship between these skull changes and iron deficiency anemia was first indicated by Eng[5] in 1958. He reported cortical thinning and diploic widening in the frontal and parietal bones of a twelve year old girl, and published the results of an extensive examination of her blood. Hemoglobin analysis revealed a normal amount of alkali-resistant hemoglobin and no abnormal hemoglobin. There was, however, severe hypochromic microcytic anemia and erythroid hyperplasia of the sternal marrow, with iron depletion. It was presumed that similar marrow hyperplasia occurring in the skull produced the changes seen roentgenographically. The patient felt well after treatment with iron preparations and the hematologic indices returned to normal. In 1960, Shahidi and Diamond[11] reported 3 cases of iron deficiency anemia with skull changes simulating the hemolytic anemias, and, later the same year, Britton, Canby, and Kohler[2] added 5 cases to the literature. This report will describe the skull changes in 7 patients with iron deficiency anemia recently seen at the Kings County Hospital Center.

REPORT OF CASES

CASE I (Fig. 1, *A* and *B*). A Negro girl, nineteen months old, was admitted to the hospital because of coryza, cough, and fever of three days' duration. She had been born at term weighing six pounds seven ounces and was one of twins. At the time of admission, she was pale and malnourished, her face was puffy and there were prominent bulges over the frontal and parietal bones. The liver and spleen were enlarged.

Examination of the blood revealed a microcytic hypochromic anemia with a hemoglobin concentration of 3.5 gm./100 ml. Skull roentgenograms showed widening of the diploic space in the frontal and parietal bones, trabecular atrophy and thinning of the tables. She received transfusions of packed red blood cells and was sent home.

CASE II (Fig. 2). A Negro girl, thirteen months old, was admitted in acute respiratory distress, with a cough and fever. She had been born with a twin at term weighing four pounds fifteen ounces. Gestation had been complicated by frequent maternal episodes of vaginal bleeding resulting in significant maternal anemia. The child's diet had contained milk and solids but was devoid of meats and nutritional supplements.

On admission, the child was pale and had an enlarged liver. Hemoglobin concentration was 4.0 gm./100 ml. Skull roentgenograms revealed widening of the diploic space in the frontal bone, with trabecular atrophy.

CASE III (Fig. 3, *A* and *B*). A Negro boy, who had been born at seven months' gestation weighing three pounds six ounces, had been fed exclusively with evaporated milk formula. At twelve months of age, the child was taken to a

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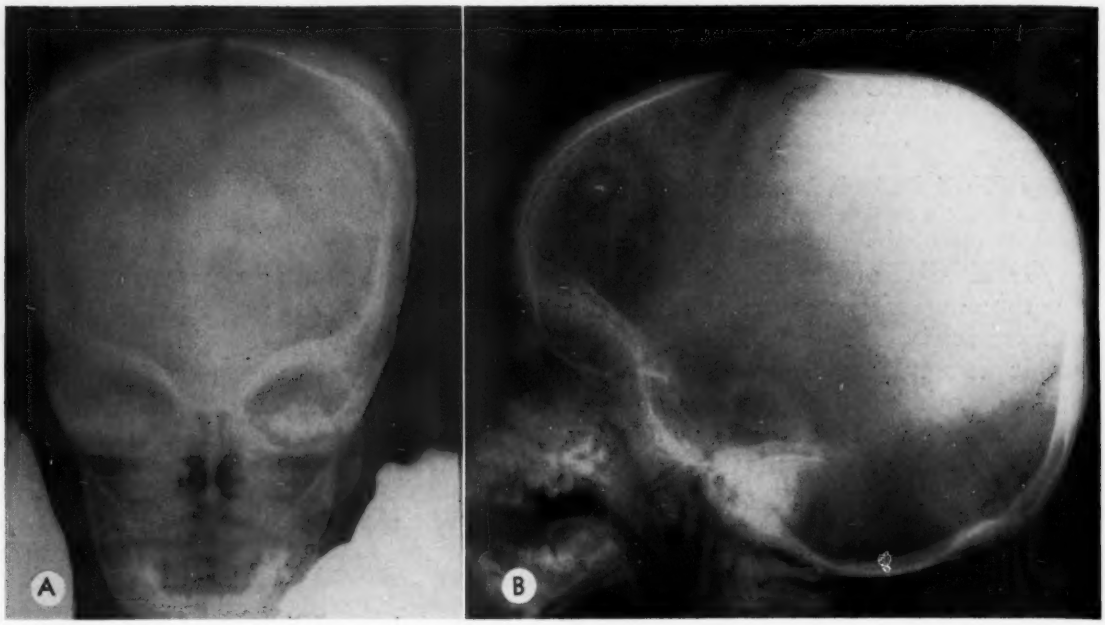

FIG. 1. Case I. (*A* and *B*) Skull roentgenograms reveal marked trabecular atrophy with thinning of the tables and widening of the diploic space. Changes are most marked in the parietal bones, in which vertical striations are noted.

health station for a periodic examination. Following the advice of the examiner, the child was brought to the hospital.

At the time of admission, the child was pale and underdeveloped. His eyelids and legs were puffy. His head was distorted by prominences in the parietal regions.

Hemoglobin concentration on admission was 3 gm./100 ml. Roentgenograms of the skull demonstrated a widened diploic space in the frontal and parietal bones, with atrophy of the outer table in the medial part of the midparietal bones.

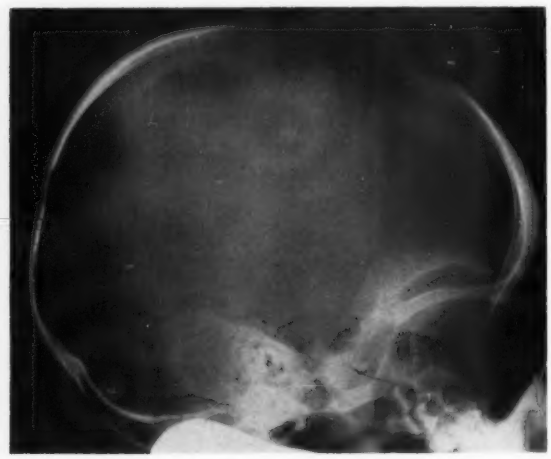

FIG. 2. Case II. Lateral view of the skull reveals trabecular atrophy in the frontal bone, with widening of the diploic space.

CASE IV. A Negro boy, aged fourteen months, was admitted to the hospital because of respiratory distress and coryza of two days' duration. He had been born at term weighing four pounds four ounces. Evaporated milk formula comprised his diet almost exclusively.

On admission the child was pale and underweight and had an enlarged liver. Hemoglobin concentration was 1.4 gm./100 ml. Skull roentgenograms revealed widening of the diploic space in the frontal and parietal bones, with mild trabecular atrophy and thinning of the outer tables.

CASE V. A twenty-four month old Negro boy was brought to the emergency room for treatment of an insect bite and was admitted to the hospital because of pallor. The child had been born at term weighing six pounds. He had been fed milk exclusively since birth. Hemoglobin concentration was 3.3 gm./100 ml. Skull roentgenograms revealed widening of the diploic space and thinning of the outer table of the parietal bones.

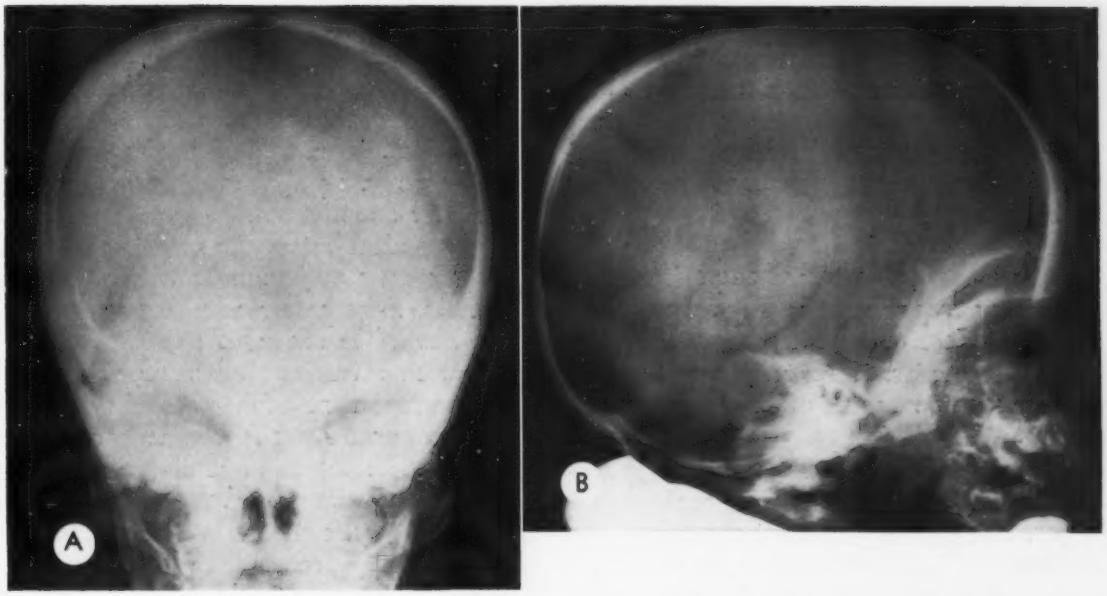

Fig. 3. Case III. (*A* and *B*) Skull roentgenograms reveal the widened diploic space in the frontal and parietal bones with considerable thinning of the outer table in the medial part of the parietal bones.

Case VI. A Negro girl, ten months old, was admitted because of fever and cough. The child had been born at term weighing six pounds and three ounces. Her diet consisted of evaporated milk formula.

On admission, the child was underweight and underdeveloped. She was unable to sit without support.

Hemoglobin concentration was 7.8 gm./100 ml. Skull roentgenograms revealed a widened diploic space, marked thinning of the outer table, and trabecular atrophy involving the parietal bones to a greater extent than the frontal bones.

Case VII. A Negro boy, aged twenty-four months, was admitted because of a scalp and ear infection. A birth and dietary history could not be obtained. The child had been abandoned by his parents and was being cared for by a neighbor.

Hemoglobin concentration on admission was 6.5 gm./100 ml. Skull roentgenograms revealed a widened diploic space in the frontal and parietal bones.

The diagnosis of chronic iron deficiency anemia in these 7 patients was established by the demonstration of hypochromic microcytic red blood cells and by the subsequent rise in hemoglobin concentration following iron therapy.

Review of All Reported Cases of Iron Deficiency Anemia with Skull Changes

Comparisons among the 16 reported patients with iron deficiency anemia and skull changes may be summarized as follows:

Birth History. Half of the children were born prematurely; half were born with a twin.

Diet. A majority of the children had a dietary intake restricted to milk.

Physical Findings. Almost all of the children were poorly developed and poorly nourished. Many had palpable cranial bossing. Half of the children had moderate enlargement of the liver and spleen. Two children had edema of the face and eyelids.

Hematologic Considerations. The hemoglobin concentration, before therapy, ranged from 1.4 to 7.8 gm./100 ml. Serum iron determinations (not performed in patients reported in this paper) were below 50 μgm./100 ml. No evidence of increased erythrocyte destruction, abnormal hemoglobins, or increase in alkali-resistant hemo-

globin was found. Bone marrow studies, when performed, revealed marked erythroid hyperplasia and increased iron binding capacity.

Roentgen Findings. The long bones examined roentgenographically were found to be normal.

DISCUSSION

Marrow hyperplasia is a striking manifestation of the chronic hemolytic anemias. The anatomic structures responsible for the roentgen appearance of marrow hyperplasia have been carefully studied. Cooley, in 1927,[10] and, subsequently, Caffey[3] described necropsy findings in thalassemia major. The diploic spaces of the calvarium are widened and filled with "sponge-like marrow traversed by bony trabeculae running at right angles to the tables." Both tables are atrophic, particularly the outer table. The calvarium, the mandible, and the facial bones, as well as the axial skeleton and appendages, are similarly involved. Cooley's explanation of the bone changes is that they are "the result of the reaction of marrow to prolonged overstimulation as a consequence of chronic hemolysis, beginning before the cortex is too firm to permit overgrowth of marrow."[3]

The roentgen appearance of marrow hyperplasia results from the expansion of young bone by an overstimulated marrow. In the first few weeks of normal life, erythropoiesis is relatively inactive.[6] As a consequence, the hemoglobin level in a normal newborn begins to fall soon after birth and may reach a minimum level in one to two months.[10] The relative hypoxia, and other stimuli, initiate active erythropoiesis. In the presence of anemia, the erythropoietic response is exaggerated and the degree of response is, in general, related to the severity of the anemia. The overactive erythropoiesis is manifested largely as marrow hyperplasia. A latent period of several months occurs between the clinical onset of anemia and the roentgen evidence of marrow hyperplasia. Caffey[3] has described the roentgen appearance of marrow hyperplasia as early as three months after the onset of anemia.

Roentgen evidence of marrow hyperplasia occurs when severe anemia has an early onset. The age of patients at the time of the initial appearance of congenital hemolytic anemias varies somewhat. Several congenital hemolytic syndromes, such as thalassemia major and congenital spherocytosis, may be present at, or shortly after, birth.[6] On the other hand, hemolytic anemias characterized by the production of an abnormal type of hemoglobin are delayed in onset by the presence of large amounts of fetal hemoglobin. Sickle cell anemia is a prime example of this latter type of hemolytic anemia, with the onset of anemia usually occurring after six months of age.

Iron deficiency anemia may occur early in life and, in many instances, is severe. It is defined as a transition from a normocytic, normochromic "blood picture" to one that is microcytic, hypochromic, and it responds to treatment with iron.[13] Infants and growing children require iron for increase in blood volume and myoglobin volume, and for respiratory enzymes which are required by all cells. It is felt that normal growing children maintain only a slightly positive iron balance. Inadequate iron in the diet or inadequate absorption of iron can readily result in iron deficiency.[8] In the absence of adequate exogenous iron sources or adequate iron absorption, the exhaustion of endogenous iron reserve can occur two to three months after birth,[10] resulting in the onset of iron deficiency anemia.

Several clinical investigations have emphasized the predisposing factors in iron deficiency anemia. In a study of 272 cases of iron deficiency anemia, Woodruff[12] found a birth weight distribution which was considerably less than average, with a high incidence of twins and premature births. Dawson and Desforges[4] also found a predominance of premature infants and twins. In addition, maternal iron depletion and inadequate diet appeared to play major

roles in the production of iron deficiency anemia. In over half the cases reviewed, two or more of the above factors contributed to anemia. In instances where one factor was important, this was most frequently a deficient diet. In a review of antenatal factors contributing to infant blood disorders, Potter[9] cites anemia from blood loss *in utero*, and anemia from blood destruction by infections and antibodies. These blood losses may increase the severity of subsequent iron deficiency anemia. The above studies indicate that low birth weight, most profound in the presence of twinning and prematurity, results in a relatively greater growth rate and nutritional requirement. Antenatal loss of iron, either by maternal or fetal iron depletion, reduces endogenous iron stores. In the absence of these predisposing factors, a diet deficient in iron appears to be the most important cause of iron deficiency anemia.

Caffey[3] has described the skeletal changes in thalassemia major in comparison with those in other chronic hemolytic anemias. The earliest change in the skull is described as widening of the diploic space—initially, in the inferior squamosal portion and horizontal plate of the frontal bone and, subsequently, in the parietal bone. Diffuse osteoporosis and trabecular atrophy occur, with thinning of the tables, more marked in the outer table. Later, coarse trabeculae, oriented as vertical striations, appear in the posterior frontal and anterior parietal bones.

As a rule, the most severe clinical cases develop the earliest and most marked bone lesions. However, in patients of the same age, with similar clinical and hematologic findings, surprising differences in the roentgen findings in the skull are encountered. Caffey[3] concluded that in thalassemia major "the skull alone is not necessarily a reliable criterion of the presence of (hemolytic) disease, nor is it an index of the degree of involvement of the remainder of the skeleton." In other chronic hemolytic anemias the changes in the skull vary even more widely. In many instances, the roentgen findings are identical with the early changes described in thalassemia major—widening of the diploic space in the frontal bone with diffuse osteoporosis and trabecular atrophy; occasionally, however, the parietal bones are involved to a greater extent than the frontal bones.

The reported patients with skull changes in chronic iron deficiency anemia have demonstrated the same variability in appearance as in the chronic hemolytic anemias. A comparison of the skull roentgenograms reproduced in this paper reveals considerable variation in the severity of bony changes as well as differences in the sites of most marked involvement. Siblings of the children, many of whom had equally severe iron deficiency anemia, had no skull changes. Many children admitted to the Kings County Hospital Center with profound iron deficiency anemia had no discernible skeletal abnormalities. It is evident that in both chronic hemolytic anemia and in chronic iron deficiency anemia the skull is an unpredictable and unreliable index of the presence or severity of anemia.

Aside from marrow hyperplasia in the chronic hemolytic anemias and chronic iron deficiency anemia, skull changes have been reported in 2 patients with congenital cardiac anomalies associated with cyanosis and polycythemia.[1] Simulators of marrow hyperplasia in the skull[2] are rickets, pseudohyperparathyroidism, infantile cortical hyperostosis, and idiopathic hypercalcemia. No problem should be encountered in clinical differentiation.

SUMMARY

Marrow hyperplasia in young, yielding skull bones causes widening of the diploic spaces and thinning of the outer tables. These roentgen findings were originally attributed to the marrow hyperplasia of chronic hemolytic anemias but they recently have been reported in 9 children with chronic iron deficiency anemia. This report adds 7 children to those reported with skull changes in iron deficiency ane-

mia. Like chronic hemolytic anemias, iron deficiency anemia may occur early in childhood in a severe form. Anemia invokes an exaggerated erythroid response, manifested largely as marrow hyperplasia. The skull changes of marrow hyperplasia vary considerably in different children and do not reflect the severity of anemia.

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HYDRANENCEPHALY: PLAIN FILM FINDINGS*

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HYDRANENCEPHALY is an anomaly consisting of complete or nearly complete absence of the cerebral hemispheres with intact meninges and skull.[8] The resulting cavity is filled with cerebrospinal fluid. This condition, an autopsy curiosity a few years ago, is being diagnosed now during life by means of transillumination of the skull[7] and special roentgenologic procedures such as ventriculography and carotid angiography.

A recent case of hydranencephaly, for which we had only plain skull roentgenograms (Fig. 1 and 2), caused us to review the literature. We could not find any illustrations of plain skull roentgenograms for cases of hydranencephaly, despite the fact that they are diagnostic and that it would be helpful to know the specific findings.

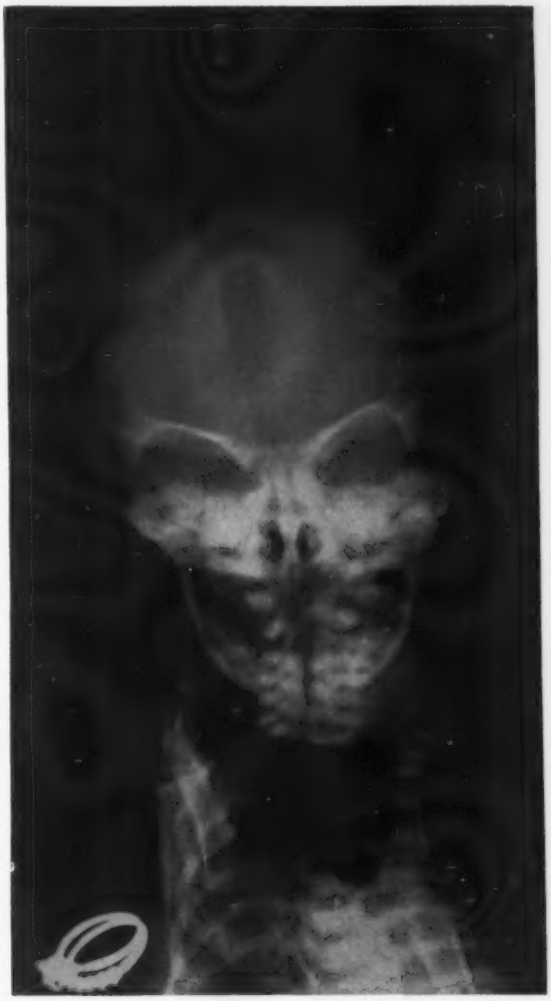

FIG. 1. Anteroposterior roentgenogram of the skull of a newborn infant with proved hydranencephaly. The apparent widening of the suture in the normal-sized skull is due to incomplete ossification of the calvarial bones.

ILLUSTRATIVE CASE

Our case was an infant, delivered with a breech presentation, who cried after birth and who presented a Bell's palsy, because of which skull roentgenograms were obtained two hours after birth. The anteroposterior and lateral views showed normal measurements (head circumference, 35.5 cm.; chest circumference, 37 cm.), thinning of the inner table, undifferentiated external table at the frontoparietal areas, and prominent suture and fontanelle width.

The infant died twenty-four hours later and at autopsy the cerebral hemispheres were found to be missing; they were represented by two small buds of brain tissue lying over the intact pons and cerebellum. The meninges were intact and filled with fluid which was not under pressure.

DISCUSSION

In addition to transillumination[3] and flat line electroencephalography,[1] plain skull roentgenography, ventriculography and carotid angiography are the roentgenologic procedures of choice, depending on the degree of underdevelopment of the hemispheres.

In ventriculography,[2] 300 cc. of cerebrospinal fluid is replaced by oxygen and usu-

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FIG. 2. Lateral roentgenogram of the skull in the same case as in Figure 1. The skull measurements are within normal limits. There are no signs of increased intracranial pressure.

ally an enormous cavity with a fluid level is demonstrated. There is ordinarily no evidence of ventricular pattern or cerebral cortex. Inverted, vertical and lateral views sometimes show residual, nondeveloped cerebral tissue in the posterior fossa or frontal region.

The carotid angiogram[4] usually demonstrates an anterior cerebral artery, essentially normal in position but with slight straightening of the ascending segment. The medial cerebral artery lies closer to the base of the skull and, on the anteroposterior roentgenogram, shows a curvature of the proximal segment with downward convexity.

The findings on the plain skull roentgenogram,[7] the ones we like to stress, are: a normal-sized skull for the infant's age, although sometimes slightly larger[9] or slightly smaller[6] than normal; and incomplete ossification of the calvarial bones suggesting separation of the sutures and widening of the fontanelle—features which, however, are only apparent.

This particular aspect of the skull in hydranencephaly demonstrates a developmental anomaly caused by the lower pressure exerted by the fluid (and meninges) on the skull than the brain would exercise. For the same reason, an anencephalic would not develop a calvarium, and a hydrocephalic would develop thin skull bones, with separated sutures and a marked increase in skull size.

SUMMARY

The roentgen diagnosis of hydranencephaly is discussed briefly in connection with the plain skull roentgenograms of a proved case. No similar roentgen studies are known to have been published. The plain roentgenography skull findings in hydranencephaly are summarized as follows: skull size within normal limits for the infant's age; marked thinning of the inner table, without osteolysis; undifferentiated external table at the frontoparietal areas; apparent widening of sutures and fontanelle and, sometimes, the presence of cystic shadows projecting over the frontoparietal areas and corresponding to the cerebral ventricles.

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MENINGIOMA OF THE POSTERIOR FOSSA IN A CHILD*

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MENINGIOMAS are tumors rarely seen before adolescence. Bailey *et al.*[1] reported 2 meningiomas in a series of 100 tumors of childhood. Globus *et al.*[6] found 2 meningiomas in a series of 92 tumors of childhood and adolescence, and Cuneo and Rand[3] encountered 2 in a series of 83 intracranial tumors in childhood. Bergstrand *et al.*[2] reported 2 meningiomas among 293 brain tumors in children, Ingraham and Matson[8] found 1 in 313 intracranial tumors in children, and Paillas *et al.*[10] reported 2 among 293 brain tumors in children.

A case of meningioma of the posterior fossa in a child with calcification as a chief finding is being reported.

REPORT OF A CASE

This four year old Puerto Rican female was transferred from another hospital with a history of generalized convulsive seizures of one month's duration. While in the other hospital, she had also developed ataxia. Physical examination upon admission revealed nystagmus on left lateral gaze, left peripheral facial paresis, left facial hypalgesia, and a diminished left corneal reflex. The deep tendon reflexes were hyperactive bilaterally. The finger to nose test was impaired bilaterally but more so on the left.

Roentgenograms of the skull revealed a large area of fine calcification, posterior and inferior to the left petrous bone, best seen on the sagittal roentgenograms (Fig. 1 and 2), which appeared to be made up of radiating strands.

A suboccipital craniotomy disclosed a finely granular, moderately vascular tumor arising from the posterior surface of the left petrous bone, extending almost to the midline and displacing the pons and brainstem to the right. An incomplete removal was performed. The pathologic diagnosis was fibrocytic meningioma.

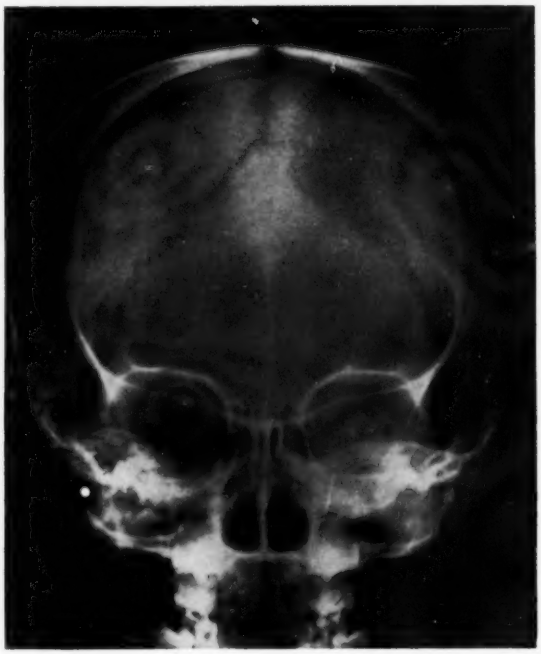

FIG. 1. Posteroanterior roentgenogram showing the area of calcification through the left bony orbit.

DISCUSSION

Meningiomas arising in the posterior fossa are infrequent at any age. Grant[7] found only 3 meningiomas of the posterior fossa in a series of 149 intracranial meningiomas. In Olivecrona's[9] series of 4,185 cases of verified brain tumors, there were 68 cases of meningioma of the posterior fossa, representing 1.7 per cent of all cases. The ratio of posterior fossa meningiomas to all intracranial meningiomas was 1 to 12. Cushing and Eisenhardt[4] found a ratio of 1 to 13 in their series of 295 intracranial meningiomas. They called attention to the difference in area between the subtentorial and supratentorial dura, stating that the

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Fig. 2. Occipital roentgenogram showing the calcification arising from the medial two-thirds of the left petrous bone.

subtentorial dura measures 166 sq. cm. while the supratentorial dura measures 754 sq. cm.

In a series of 273 tumors in children French[5] found 7 meningiomas, 2 of them subtentorial. Tristan and Hodes[11] had only 1 patient under ten years of age in 59 cases of posterior fossa meningioma.

Calcification has been frequently described in supratentorial meningiomas in children and in meningiomas of the posterior fossa in adults; however, in a review of several large series of infratentorial meningiomas in children, calcification has not been mentioned as a finding.

SUMMARY

A case of meningioma of the posterior fossa in a child is reported. In this patient marked calcification was noted in the tumor. Calcification in such meningiomas, while fairly common in adults, appears to be an unusual finding in children.

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INTRACRANIAL CALCIFICATION IN INFANTS*

IS IT POSSIBLE ROENTGENOGRAPHICALLY TO DISTINGUISH BETWEEN TOXOPLASMOSIS AND CYTOMEGALIC INCLUSION DISEASE?

By ARTHUR S. TUCKER, M.D.
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CALCIFICATIONS of the brain in infants can almost always be considered to be of inflammatory origin. Tumor and physiologic origins of calcified brain tissue are almost unheard of in the first few years of life. Of the inflammatory processes causing intracranial calcification in infants, toxoplasmosis is easily the most common. Hundreds of cases have been reported since the identification of *Toxoplasma* as a human pathogen by Wolf, Cowen, and Paige in 1939.[7]

The most helpful single finding in diagnosing toxoplasmic infection is the presence of chorioretinopathy. Other conditions encountered frequently enough to form with chorioretinopathy a tetrad of diagnostic features are cerebral calcification, hydro- or microcephaly, and psychomotor disturbances. The diagnosis is best substantiated by serologic studies. Of these, the most practicable in most instances is the dye test for antibodies. In some cases, complement fixation is a useful adjunct, although this antibody develops more slowly and disappears more rapidly than the dye test antibody.

The calcifications in toxoplasmosis commonly are in foci scattered through gray and white matter. Apart from a tendency to be more numerous in the posterior than in the anterior part of the brain (Fig. 1 and 2), the distribution of the calcifications covers a wide area. Dyke *et al.*[3] in 1942 pointed out that a most characteristic but, unfortunately, not most common distribution was in curved streaks in the basal ganglia and thalami (Fig. 3).

In recent years, the reports on toxoplasmosis as a cause of intracranial calcification have been outnumbered by those describing a new disease of virus etiology commonly called cytomegalic inclusion disease. In this infection of the newborn child, there always is jaundice, and the clinical manifestations, particularly as related to the eyes and central nervous system, may be indistinguishable from those described in toxoplasmosis. Intracranial calcifications may be present and, as in toxoplasmosis, the lesions are apt to be multiple scattered foci. Other organ systems of the body are commonly involved, and the liver and spleen invariably show severe effects of the infection. The diagnosis is frequently made by finding inclusion cells in the urine, gastric washings, or other secretions.

FIG. 1. Skull roentgenogram of a three and one-half year old female shows scattered foci of calcification, principally in the posterior part of the brain. The child had a mild microcephaly, with bilateral central choroiditis, and an I.Q. of 51.

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DIFFERENTIAL DIAGNOSIS

Although cytomegalic inclusion disease is a much less common cause of widely distributed intracranial calcifications than is toxoplasmosis, a differential diagnosis between the two may be difficult. The dye test may not provide an immediate answer regarding toxoplasmosis, partly because it involves sending serum to one of the laboratory centers equipped to perform the test, but principally because a positive titer in a newborn infant is meaningless if the mother has been infected.

Cytomegalic inclusion disease may be equally difficult to prove if inclusion cells are not readily spotted in the excreta of the infant. The radiologist, therefore, may be asked whether there is anything about the lesions in the brain which will weigh in favor of one or the other diagnosis.

FINDINGS REPORTED IN THE LITERATURE

Several articles have suggested that a systematic arrangement of calcification lining the lateral ventricles may be helpful in favoring a diagnosis of cytomegalic inclusion disease. Mercer, Luse, and Guyton,[5] in their case report of the first patient to be diagnosed during life, state, "Ventriculograms confirmed impression that these areas of calcification were primarily in relation to ventricular walls."

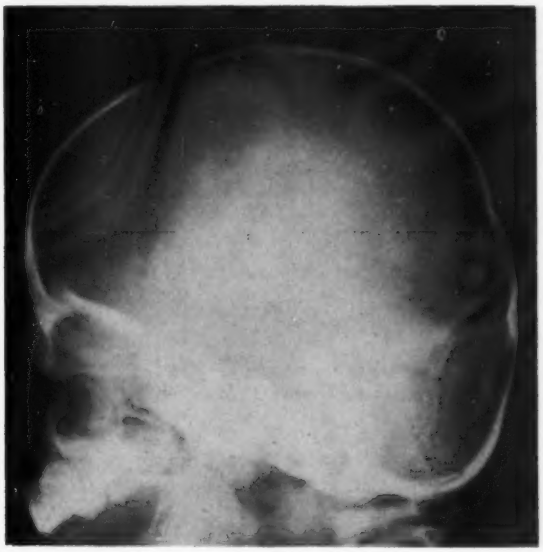

Fig. 2. Skull roentgenogram of a six month old female shows scattered foci of calcification in approximately a periventricular distribution, but air studies were not performed for exact localization. The clinical features were microcephaly, spastic seizures, and retinitis.

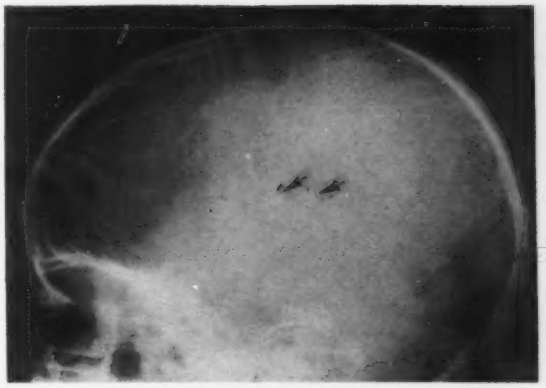

Fig. 3. A five and one-half year old male with a history of convulsions since the age of three. The patient was severely retarded, unable to talk or feed himself, and could walk only with assistance. Hearing and visual perception were markedly limited. He had the habit of hitting his head against the wall. The skull roentgenogram shows streaks of calcification (arrows) which are rather characteristic of toxoplasmosis.

Haymaker *et al.*[4] reported a case with advanced periventricular calcification, and concluded, "It seems likely that mental deficiency associated with periventricular calcification may in some instances be due to cytomegalic inclusion disease."

Sackett and Ford[6] showed extensive calcification of the linings of the ventricles in their case report. They apparently missed seeing the article by Haymaker *et al.* for they say, "Demonstration of the outline of the lateral ventricles of the brain on a RG of the skull is illustrated. This is the second such case reported, and in both the autopsy confirmed the impression of generalized cytomegalic inclusion disease."

Some recent articles are more emphatic. Daurelle, Smith, and Riemer,[2] in 1958, reported a case with calcium outlining the walls of the lateral ventricles, and suggested "that this radiographic finding, when pres-

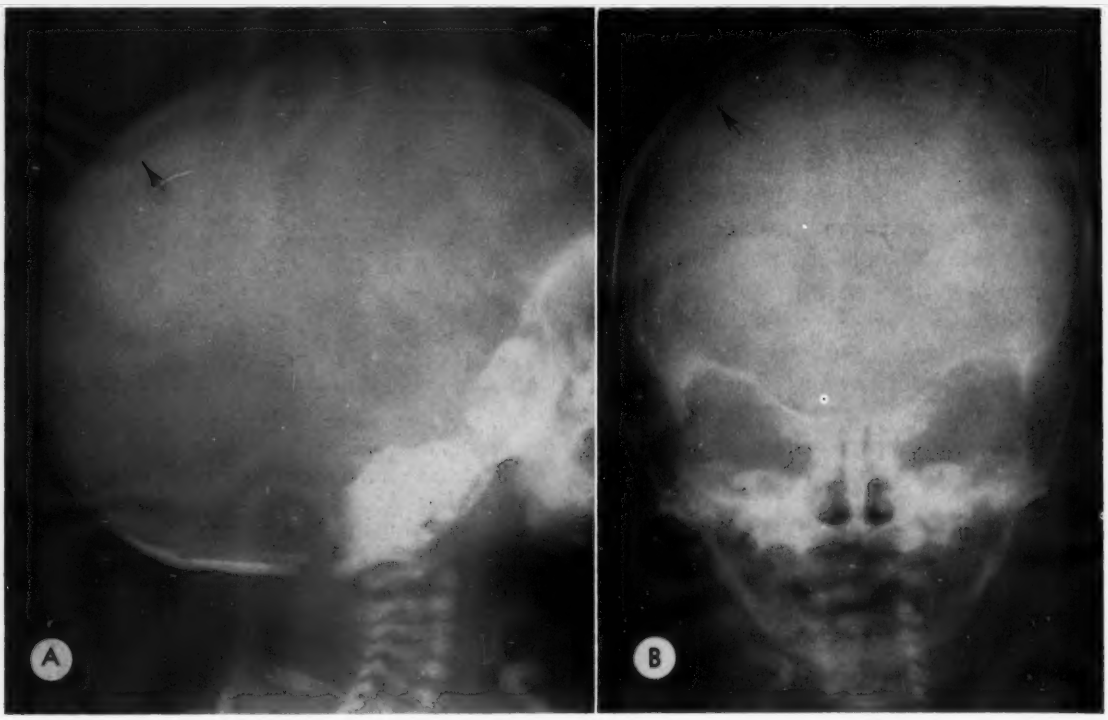

FIG. 4. (*A* and *B*) Calcification is seen in a distinct layer approximately 3 cm. within the calvarium and down the longitudinal fissure (arrows).

FIG. 5. Formalin-fixed brain, sectioned longitudinally. The parietal and occipital cortex was severely thinned, and the posterior parts of the lateral ventricles were so dilated that their walls collapsed and infolded upon sectioning. Arrows point to flakes of calcium in the ependymal lining of the dilated ventricles.

ent, indicates a diagnosis of cytomegalic inclusion disease, and may be pathognomonic of the disease."

Allen and Riley[1] at about the same time reported 2 cases, 1 of which showed calcification outlining dilated lateral ventricles, and they concluded, "Visible calcification outlining dilated lateral ventricles is probably pathognomonic when it occurs."

In the light of these experiences, we were presented with a case which exhibited extensive intracranial calcification.

REPORT OF A CASE

A premature male weighing 1,800 gm. was the product of a thirty-two week pregnancy. Routine physical examination at four hours had

revealed hepatosplenomegaly, and a blood smear showed a marked decrease in platelets. Upon admission at sixteen hours to Babies and Childrens Hospital there was, in addition, evidence of slight jaundice, and many petechiae scattered in clusters over the body. Coombs' test was negative. The jaundice rapidly became more severe. Exchange transfusion was started, during which the infant died at twenty-five hours of age.

Antemortem skull roentgenograms demonstrated calcifications of both hemispheres, principally in symmetric layers slightly within the cortex (Fig. 4, *A* and *B*). Autopsy revealed diffuse involvement of the organs by toxoplasmosis. Examination of the brain (Fig. 5 and 6) showed that the distribution of calcium was due to marked hydrocephalus, with lime deposited primarily in the ependymal lining.

CONCLUSION

On the basis of an autopsy diagnosis of toxoplasmosis of a newborn infant with a layer of calcium lining the dilated lateral ventricles, we are unable to substantiate any roentgenographic feature which can be considered to be pathognomonic of cytomegalic inclusion disease.

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The author gratefully acknowledges the assistance of Dr. Robert P. Bolande in providing photographs from which Figures 5 and 6 were prepared.

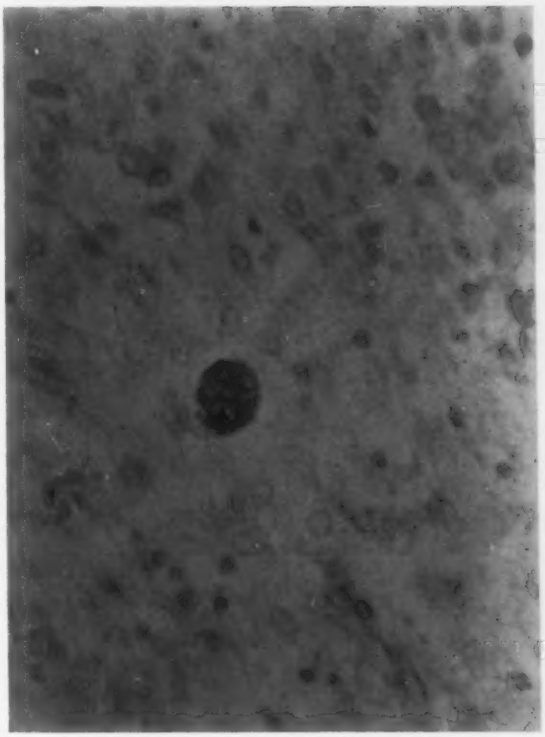

FIG. 6. Histologic section of the brain cortex of the patient shown in Figures 4 and 5. The *Toxoplasma* parasite is conspicuous.

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SPONDYLO-EPIPHYSEAL DYSPLASIA (PSEUDO-ACHONDROPLASTIC TYPE)*

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IN a classification of skeletal dystrophies, spondylo-epiphyseal dysplasias are said to comprise a subgroup of hereditary chondrodystrophies which is characterized by epiphyseal and vertebral modifications, of which the best known form is Morquio's disease.[2] As a rule, there would appear to be little opportunity for confusion between Morquio's disease and the well-known achondroplasia. In fact, the short trunk and relatively long extremities in cases of the former are considered to contrast with the relatively long trunk and short extremities in the latter condition.

Recently, Maroteaux and Lamy[3] reported observations in 3 dwarfed individuals who demonstrated features resembling achondroplasia but who, they believe, actually represented an extreme form of spondylo-epiphyseal dysplasia. The authors emphasize the fact that actual shortening of the extremities is frequent in Morquio's disease and can, at times, be so much accentuated as to cause confusion in diagnosis. The extreme form of spondylo-epiphyseal dysplasia, the pseudo-achondroplastic type, is demonstrated by the 3 patients who are the subjects of the present report.

REPORT OF CASES I AND II

CASE I. D.L.H., born September 17, 1936, was first seen at eight years of age in the Orthopedic Clinic at the Cincinnati General Hospital because of a painful left hip, dwarfism, and obesity. At birth, the patient weighed 6 pounds 4 ounces and was considered to be a normal full-term infant. She walked at ten months of age, talked normally and was an alert child. At approximately four to five years of age, she was observed to have a waddling gait and, at this time, it was also noted that she was appreciably shorter than other children of her age.

At the time of her first visit in the hospital, the patient was described as "dwarfed" with predominant shortening of the extremities and a relatively normal length of the trunk. She was obese and had an accentuated lumbar lordosis and scoliosis. She walked with a waddling gait. Her face and cranium were normal in appearance. The diagnosis of achondroplastic dwarfism was made. At the age of twelve years (Fig. 1, *A* and *B*), she was seen in the Endocrine Clinic at Children's Hospital because of the obesity and dwarfism. Shortly afterward, following mild trauma at an amusement park, she began to develop progressive quadriparesis and ultimately quadriplegia. Myelographic studies and roentgenographic examinations failed to demonstrate the local spinal complications of achondroplasia. After two cervical laminectomies and a period of convalescence, the patient stabilized with a paraplegia. Because of her normal intelligence, she was able to complete high school in spite of the neurologic handicaps mentioned. Various laboratory studies were normal including calcium, phosphorus, alkaline phosphatase, basal metabolic rate and radioactive iodine uptake. At the age of sixteen, she weighed 77 pounds and measured 39 inches in height. She is now twenty-four years of age and confined to a wheelchair.

CASE II. S.H., born May 1, 1934, was seen in the Endocrine Clinic of the Children's Hospital while accompanying his sister, Case I, to the clinic. He had been born at term as an apparently normal infant and his early development was reported as normal. His short stature and waddling gait were not noted until he was between four and five years of age. At the age of fourteen (Fig. 2, *A* and *B*), he weighed $45\frac{1}{2}$ pounds and was $36\frac{3}{4}$ inches in height. He was of average intelligence and subsequently was able to complete high school without difficulty. Be-

*From the Departments of Pediatrics and Radiology, College of Medicine, University of Cincinnati; the Children's Hospital and Children's Hospital Research Foundation; and the X-Ray Department of the First Pediatric Clinic of the Medical School of Poznan, Poland.

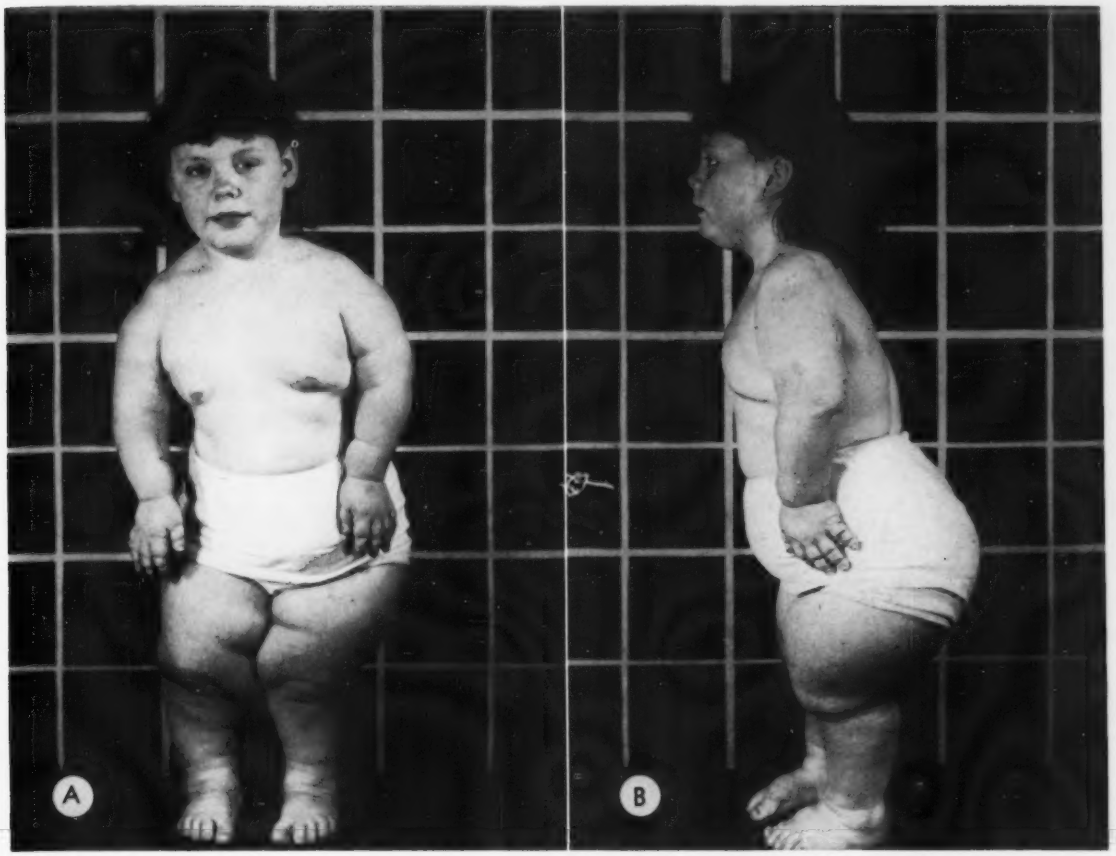

Fig. 1. Case 1. (*A* and *B*) Photographs at twelve years of age. Because of the obesity, the face may seem to have some mild achondroplastic characteristics. However, note that the features are delicate and that a true saddle nose deformity and protruding brow are not present.

cause there were no complications to his dwarfism, this patient was not examined as carefully as his sister, although we were able to obtain clinical photographs at the time of his visit and roentgenographic examinations as well. It was thought that he and his sister both suffered from achondroplasia.

FAMILY HISTORY

The mother of these 2 patients was of normal height and weight and came from a family in which dwarfism or other abnormalities of stature were denied. The father had been a "dwarf in a circus," measuring 4 feet 9 inches in height. He apparently was also a chronic alcoholic and died from the complications of this condition several years after the children were first seen. He had never been seen by a member of the hospital departments. Consanguinity was denied. Information concerning the father's antecedents and collaterals is incomplete, but the children's mother stated that she did not believe there were other affected individuals in the father's family. A pedigree, as developed from conversation with the mother, is diagrammed in Figure 3.

ROENTGENOGRAPHIC FINDINGS

Skull (Fig. 4, *A* and *B*). In both children, the skull was normal in appearance and showed no evidence of brachycephaly, frontal protuberance or bossing, or of saddle nose deformity. Abnormal shortening of the cranial base was not demonstrated. Developmental features were commensurate with the age.

Extremities (Fig. 5, *A* and *B*; 6, *A* and *B*). Severe deviations from normal were observed in all the metaphyses and epiphyses of the tubular bones including the bones of the hands. The metaphyseal areas were enlarged, irregular, and had a mushroomed appearance. The epiphyses were small, irregular, fragmented,

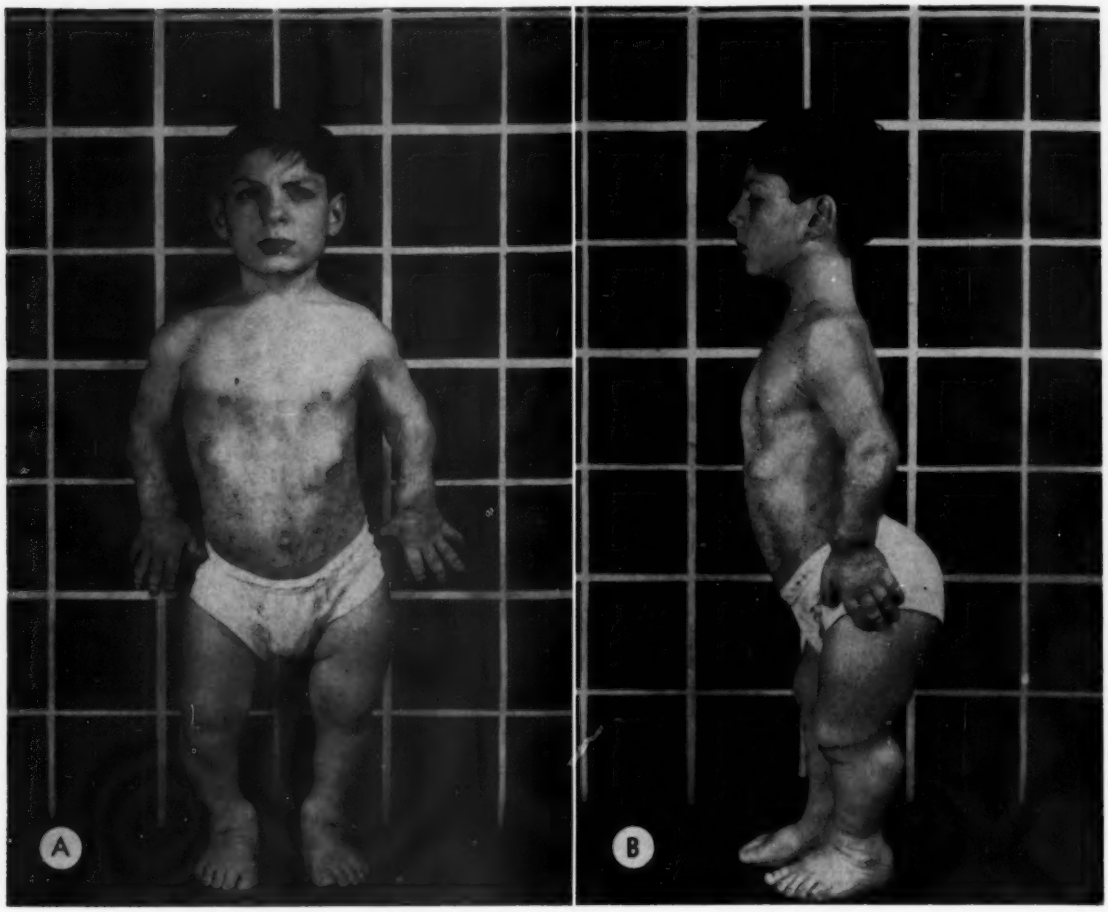

FIG. 2. Case II. (*A* and *B*) Photographs at fourteen years of age. The normal head and face are better shown on these photographs than on those of the sister (Fig. 1, *A* and *B*), although the achondroplastic proportions are prominent.

irregularly ossified and deformed. The diaphyses were shortened and tended to bow outward. The phalanges were short, wide, "stubby" and had irregular wide metaphyses. The cortices were not abnormally thickened, although the bones were relatively thick for their length.

Spine and Ribs (Fig. 7, *A*, *B* and *C*). Both patients demonstrated a rather prominent scoliosis, more marked in the girl than in the boy. The vertebral bodies were somewhat flattened and had a tendency to a biconvex form. On the lateral roentgenograms, some anterior "beaking" was visualized, particularly in the lumbar vertebrae. The ribs had a spatulate appearance produced by an increased breadth lateral to relatively normal necks. The ribs were somewhat short and their sternal ends were cupped and enlarged.

Pelvis (Fig. 8). The pelvis was small in both patients. The greater sciatic notch was not markedly reduced in size. Irregular mineralization of the femoral heads and necks and the adjacent acetabula was a very prominent feature.

REPORT OF CASE III

CASE III. A nine year old girl was admitted to the First Pediatric Clinic in Poznan, Poland, December 1, 1959, because of short stature, deformities of the upper and lower limbs, and a waddling gait. The admission diagnosis was achondroplasia. The patient was the result of the tenth pregnancy of healthy parents. The mother was thirty-seven and the father fifty-four years of age when the child was born. Only 2 brothers, results of the first two pregnancies, were living, aged twenty and twenty-

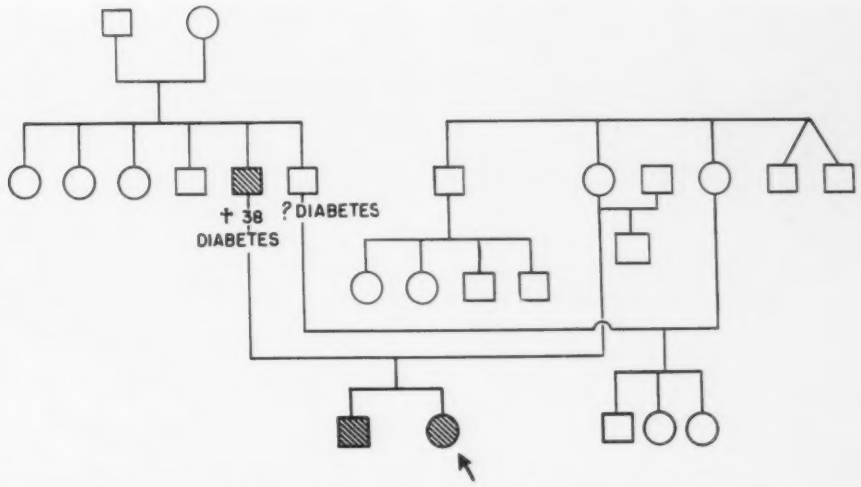

Fig. 3. Case I and II. Diagram showing pedigree which was developed from the information obtained from the patients' mother; none of the other members of the family have been examined.

two years, respectively. In the interval, there had been 6 miscarriages induced by quinine and 1 artificial premature labor. During the second month of the pregnancy with the patient, the mother ingested considerable quinine in an unsuccessful attempt to induce abortion. The amount ingested was apparently sufficient to cause intoxication.

The child weighed 3,300 gm. at birth. The length was not recorded but the child was said to be normal. She was breast-fed until the fourth month of life and subsequently was given an adequate diet. Vitamin D-2 (600,000 units) was administered on three occasions in the first year of life.

At seven months of age the mother was informed that the child was short; she had not observed any abnormality in size up to this time. Some weeks later, a slight bowleg deformity was noted. Motor development was slightly retarded. The patient sat at the age of seven months, stood up at one and one-half years and walked at three years. The mental development, however, had been normal. Talking began at eighteen months and the child was able to read and write to a degree commensurate with her age.

At the age of eight years, the diagnosis of achondroplasia was made when the child was hospitalized because of the short stature. The parents, brothers and other members of the family were of normal stature and there was no

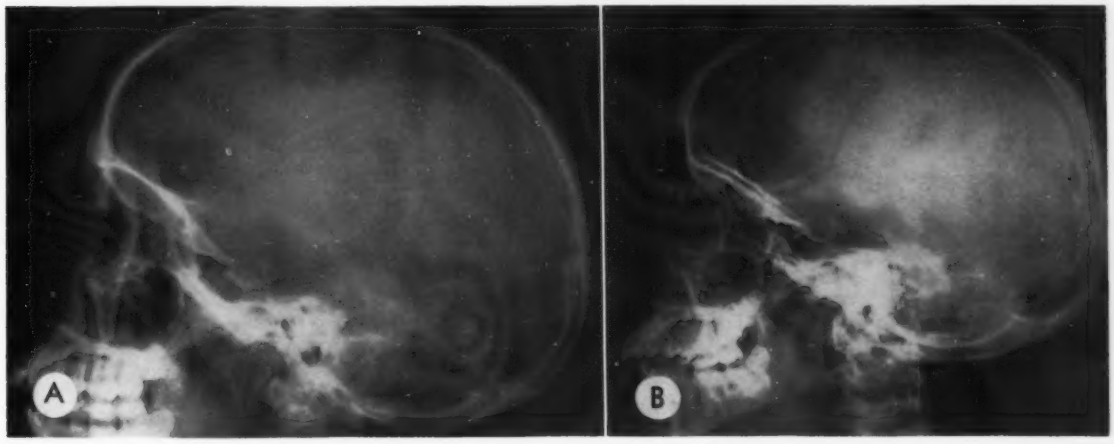

Fig. 4. Lateral skull roentgenograms of (*A*) Case I and (*B*) Case II are normal and show no evidence of achondroplasia.

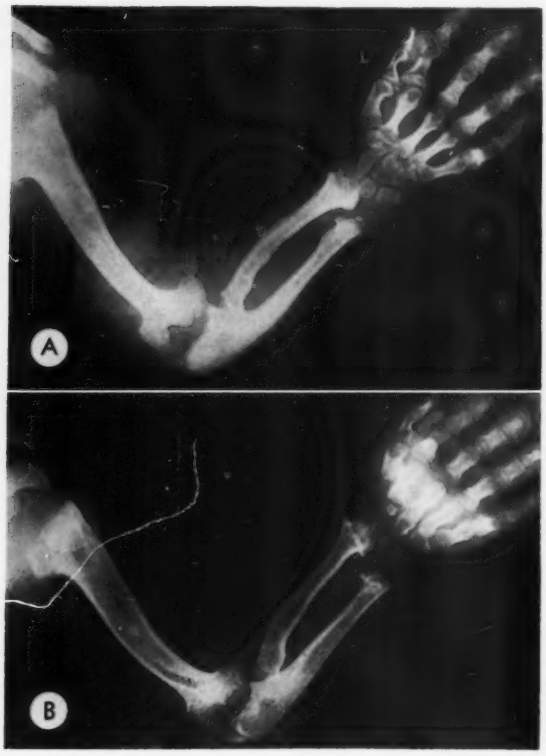

FIG. 5. Roentgenograms of the upper extremities of (*A*) Case I and (*B*) Case II show short and thick bones, excessive flaring of the metaphyses, and marked irregularity and fragmentation in the unfused ossification centers.

history of skeletal disease.

On physical examination, the child was found to be well nourished but short in stature (height —92 cm., weight—17 kg.) (Fig. 9, *A*, *B* and *C*). The upper and lower limbs were short in relation to the length of the trunk and the head. An exaggerated lumbar lordosis was present. The lower extremities were bowed and a waddling gait was present. Marked enlargement of the joints was noted. The motions of the large joints were limited. Muscle tone, volume and strength were normal. The head was normal. Examination of the ears, nose and throat revealed moderate hypertrophy of the tonsils and adenoids. The teeth were normal. The clavicles were overlong without exaggeration of the curves; some flaring of the lower thoracic cage was noted. Measurements of the upper limbs are shown in Table I.

Laboratory findings revealed a normal red blood cell count, white blood cell count and hemoglobin; urinalysis (specific gravity 1.025,

FIG. 6. Roentgenograms of lower extremities of (*A*) Case I and (*B*) Case II show the extremely irregular fragmented appearance of the ossification centers. The cortices are not abnormally thick.

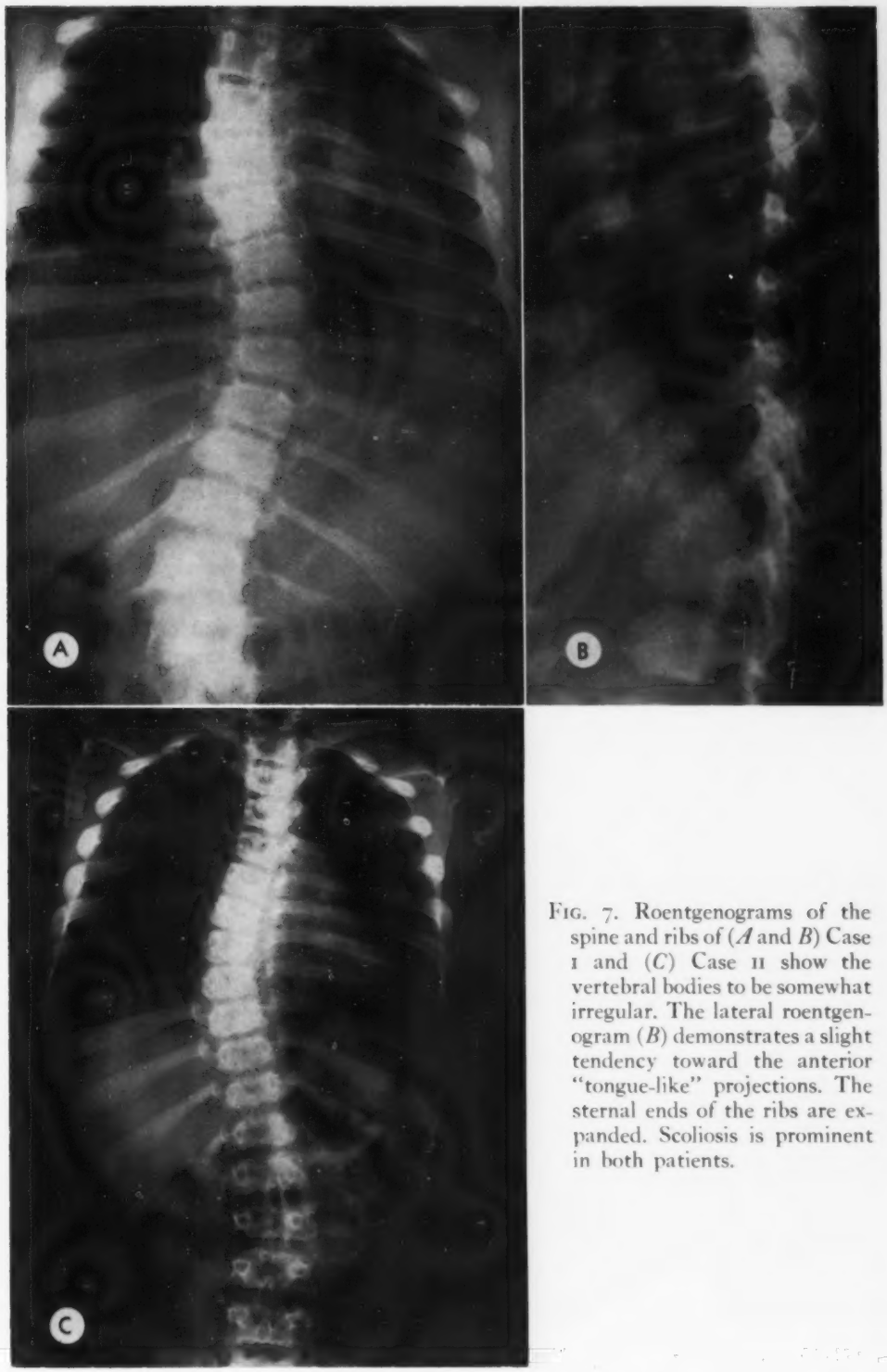

FIG. 7. Roentgenograms of the spine and ribs of (*A* and *B*) Case I and (*C*) Case II show the vertebral bodies to be somewhat irregular. The lateral roentgenogram (*B*) demonstrates a slight tendency toward the anterior "tongue-like" projections. The sternal ends of the ribs are expanded. Scoliosis is prominent in both patients.

FIG. 8. Case I. Roentgenogram of the pelvis shows only slight diminution in the length of the sacro-iliac notch notwithstanding the marked lordosis of this patient. See also Figure *6B*. Neither pelvis is that of classic achondroplasia.

TABLE I

MEASUREMENTS OF CASE III

	Length (cm.)	Normal Length* (cm.)
Upper Limb (acromion to third finger)	34	57
Forearm and Hand (radial point to third finger)	19	33
Hand (styloid point to third finger)	11	14
Sitting Height	66	66
Lower Extremities (anterior superior iliac spine to ground)	41	71
Leg (tibial point to ground)	20	34
Foot (malleolus to ground)	5	5

* These figures, corresponding to normal lengths for a nine year old female, were provided by Dr. Pierre Maroteaux.

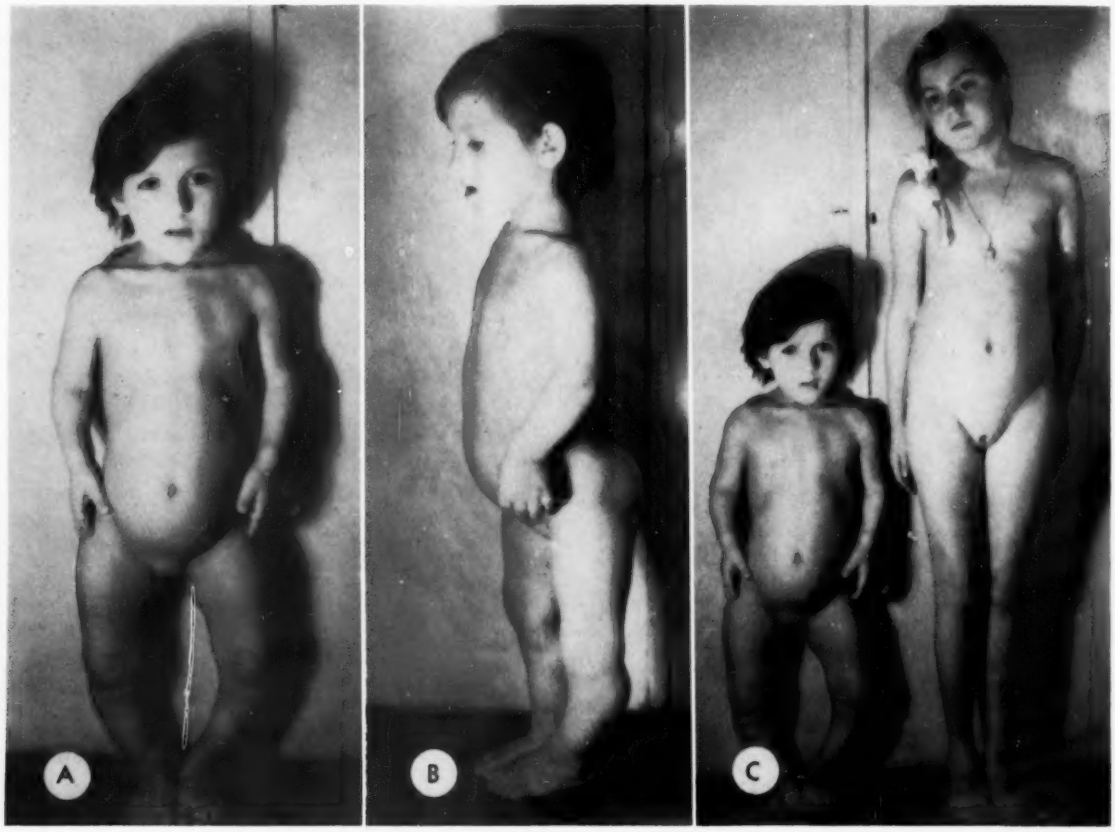

FIG. 9. Case III. Photographs at nine years of age. (*A*) Frontal view. (*B*) Lateral oblique view. (*C*) Comparison with normal female of nine years.

pH 6.9); normal blood and urine chromatography and normal excretion of calcium, phosphate and ammonia in a twenty-four hour urine specimen. The serum calcium was 10.4 mg. per cent; phosphorus 4.3 mg. per cent; serum alkaline phosphatase 11.3 Bodansky units; nonprotein nitrogen 21 mg. per cent; serum urea 30 mg. per cent; creatine 1.2 mg. per cent; cholesterol 176 mg. per cent. The serum sodium, potassium and chloride concentrations were normal. The glucose tolerance test was normal; 7 per cent fat in stool; trypsin test was positive in 1:5 and 1:10 dilutions, negative in 1:50 and 1:100. Electrophoretic protein pattern: total protein 6.2 gm. per cent, albumin 60 per cent, alpha$_1$ 4.2 per cent, alpha$_2$ 7.5 per cent, beta 9.3 per cent, and gamma 19 per cent.

An excision biopsy of the costochondral junction of the left sixth rib was performed. Only the cartilaginous portion was taken. This appeared to be grossly normal; upon section, the cells in the cartilage were noted to be irregularly disposed. Beneath the perichondrium, the cells were larger than in the deeper layers. Some free spaces were seen around the cells. The bone substance of the cartilage was swollen in several areas. In the deepest layers of the cartilage, the cells were gathered in groups of less than 20. Under the perichondrium, some small collections of capillaries were seen. No tissue characteristic of achondroplasia was noted and no connective tissue was observed at the cartilage-shaft junction.

ROENTGENOGRAPHIC FINGINGS

Skull (Fig. 10). The roentgen appearance of the skull and teeth was normal. The foramen magnum was normal in size.

Extremities (Fig. 11, *A*, *B* and *C;* and 12). Roentgen examination of the bones of the upper and lower extremities (Fig. 11, *A*, *B* and *C*) demonstrated these structures to be short and thick with otherwise normal cortex. A moderate varus deformity was present at the knees. All the normal curves of the long bones were exaggerated. The ends of the shafts were flaring, irregular and fragmented. Skeletal age of the hands and wrists was approximately five years according to the standards of Greulich and Pyle (Fig. 12). The component bones were abnormally short and thick and demonstrated irregularities in the epiphyseal and metaphyseal areas comparable to those noted in the large tubular bones.

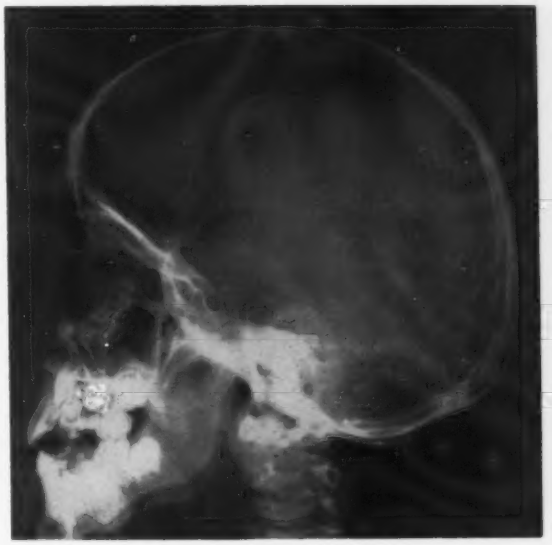

Fig. 10. Case III. Roentgenogram shows normal skull. The lack of cranial and facial involvement is an important differential point with respect to achondroplasia.

Spine and Ribs. In the spine there was a prominent lordosis. Lumbarization of the first sacral segment was present. The upper and lower borders of the lumbar vertebral bodies were irregular but no other abnormalities were found. In particular, no marked flattening of the vertebral bodies and no anterior tongue-like projections were present. On the anteroposterior roentgenogram, no distinct scoliosis was demonstrated. The scapulae were not remarkable. The ribs were of normal length and shape but irregularity of the zones of provisional calcification was noted at the costochondral junctions. The clavicles were long but the curvature was normal.

Pelvis (Fig. 13). In the pelvis the iliac bones were somewhat shortened below the posterior inferior iliac spine. The greater sciatic notches were reduced in size. The acetabular angles were flattened. The sacrum was normal in shape and the ischiopubic synchondroses were open.

DISCUSSION

The chief features, described by Maroteaux and Lamy,[3] in differentiating the pseudo-achondroplastic form of spondylo-epiphyseal dysplasia from classic achondroplasia are clearly demonstrated by these 3 cases. These include: (1) the late date of discovery of the abnormality; (2) the ab-

FIG. 11. Case III. Roentgenograms of the (*A*) upper extremity, (*B*) lower extremity and (*C*) knees show the flaring of the metaphyses, the marked irregularity of the epiphyses and the normal cortex.

sence of clinical and roentgenologic abnormalities in the face and skull; and (3) the roentgenologic findings of gross irregularities in the epiphyseal-metaphyseal areas with fragmentation of the epiphyseal ossification centers. Our first 2 patients demonstrated abnormalities in the vertebral column which were not a prominent finding in the third patient. An additional point worthy of note is the relative length of the sacroiliac notch in our patients as well as in those described by Maroteaux and Lamy.[3] This contrasts significantly with the small sacroiliac notch which has been emphasized recently by Caffey[1] as a pelvic manifestation of classic achondroplasia.

It is unfortunate that actual measurements in the newborn period are not available of any of the patients reported thus far. The delay in recognition of the disease is considered an important differential feature but is dependent exclusively on nonobjective observations by the parents. It is well known that mild or even moderate achondroplastic dwarfs may not be recognized at birth unless a clue is provided by roentgenologic examination; nevertheless, dwarfism as marked as that noted in our patients would be expected to have been recognized much earlier in life than at the end of the first year (Case III) or the third to fifth year (Case I and II) if it were caused by classic achondroplasia.

The obvious escape of involvement of the cranial structures would appear to be an extremely important differential point. Spinal complications in classic achondroplasia have been documented by Vogl and Osborne[7] and by Spillane.[6] The occurrence of signs of transverse myelopathy in our patient (Case I) was originally thought to support further the diagnosis of achondroplasia. Obviously, the complication, if a result of diminished intraspinal space, should be expected to occur in any condition in which the space is compromised, including

Fig. 12. Case III. Roentgenogram of the hands and wrists shows short stubby bones, irregularity in epiphyseal ossification centers and poor development of carpal ossification centers.

the pseudo-achondroplastic form of spondylo-epiphyseal dysplasia.

The roentgenologic features of spondylo-epiphyseal dysplasia certainly differ from those of classic achondroplasia, but experienced observers had long noted incomplete and intermediate forms which suggest transitional forms of cartilaginous dystrophies. With the present interest in enzymatic defects as the basis for disease processes, it is tempting to consider the various forms of this group of skeletal dystrophies as resulting from the various combinations of certain enzymatic processes which affect cartilage proliferation, susceptibility of cartilage matrix to calcification, and transformation of calcified cartilage to bone. If we also include factors which determine anatomic distribution and time and sequence of action[5] of the various defects, we are provided with a concept which brings together these various conditions. This, of course, takes us directly into the field of genetics, and here the studies of heredity of the several diseases may provide additional information. However, it is pertinent to point out that there are difficulties in differentiating the mutational origin of a dominant condition from the unveiling of a recessive characteristic. Moreover, it is quite possible that phenocopies (*i.e.*, nongenetic simulations of genetically determined traits) may occur in this group of malformations as well as in others. In our Case III, the mother was attempting abortion during an important developmental period. The clinical and roentgenologic findings, although similar to those of the first 2 cases and to those described by Maroteaux and Lamy, differ to some extent in the relatively unaffected spine, and

Fig. 13. Case III. Roentgenogram of the pelvis shows the marked irregularity of the epiphyseal ossification centers. The sacroiliac notch is somewhat shorter than in Cases I and II and approaches more closely the findings in achondroplasia.

the pelvis in which resembles more that of the true achondroplast. Furthermore, there is no evidence of any hereditary disease in the antecedents.

There can be little doubt of the dominant nature of disease in Cases I and II. This heredity differs from the recessive nature of the disease described by Morquio and which bears his name. In 1957, Maroteaux, Lamy and Bernard[4] reported a form of spondylo-epiphyseal dysplasia with a late onset (second decade) which they believe is transmitted by a recessive sex-linked gene. These individuals had clinical and roentgenologic findings closely resembling those of Morquio's disease. It would therefore appear that the various approaches to classification—clinical manifestations, evolution, roentgenologic features and genetic nature—are all collectively inadequate and individually misleading until a basic defect, probably biochemical, can be found. Meanwhile, however, it would appear that the description of the variants and the grouping of these variants with respect to their common features may point toward the area in which a basic defect should be sought.

SUMMARY

Three patients with a pseudo-achondroplastic form of spondylo-epiphyseal dysplasia are described. The findings conform very closely to the condition as originally reported by Maroteaux and Lamy.[3] Each patient was first considered to have classic achondroplasia. The features which differentiate spondylo-epiphyseal dysplasia from classic achondroplasia and which were present in our patients include: (1) delayed onset of dwarfism, (2) lack of involvement of the head and face, and (3) roentgenographic irregularities in the epiphyses. A fourth finding with respect to the shape of the pelvis in achondroplasia, as described by Caffey, is added to the differentiating signs.

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GARGOYLISM: A REVIEW OF THE ROENTGEN SKULL CHANGES WITH A DESCRIPTION OF A NEW FINDING*

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GARGOYLISM (Hurler's syndrome), a metabolic disorder characterized by the overproduction of certain mucopolysaccharides which accumulate in connective tissue as well as in the cells of many organs, gives rise to a distinct clinical syndrome. This entity was first recognized by Hunter[7] in 1917 and then was described in greater detail by Hurler[8] in 1920. Since that time numerous reports[3-6,9-11] have appeared in the medical literature, describing the varied aspects of this rare disorder.

The clinical syndrome is characterized by dwarfism, infantilism, mental retardation, coarse facial features, large tongue, pot belly, hepatomegaly, splenomegaly, kyphosis, corneal clouding and characteristic skeletal dystrophy. Overproduction of certain normal polysaccharides results in their accumulation in most organ systems including the nervous, cardiovascular, reticuloendothelial, endocrine, and skeletal systems and explains the protean manifestations of the disease. The excess production of these polysaccharides is accompanied by the excretion of large quantities in the urine which provides the basis for a quantitative test.[12]

Although the majority of infants with this disorder are normal at birth and develop the characteristic clinical picture toward the end of the first year of life,[14] Caffey has described the roentgen appearance of prenatal and neonatal bone lesions and their subsequent postnatal evolution.[1] When all of the stigmata are present, the disease is readily recognized, but variants, with one or more major features being absent, do occur. It is this latter group which has been confused with Morquio's disease, achondroplasia, and hypothyroidism. From the evidence currently at hand, it would appear that gargoylism is genetic in origin with at least two distinct genotypes—a sex-linked recessive and an autosomal recessive form.[12]

The roentgenologic appearance of the skeleton in gargoylism, although somewhat similar to that seen in Morquio's disease, is distinctive and a prominent feature of the clinical syndrome. In the extremities, the changes, which are more pronounced in the upper limbs, consist of swelling of the diaphyses with irregular thickening of the cortex. The ends of the bones are tapered and in the humerus the surgical neck is angled dorsad. The distal epiphyseal plates of the radius and ulna usually face toward each other. The changes in the hands consist of pointing of the base of the metacarpal bones and a "bullet-nose" appearance of the phalanges. In the lower extremities, the changes are less marked, but usually coxa valga, narrowing of the proximal one-third of the femur and poor mineralization of the femoral head are noted. A kyphotic deformity of the spine at the thoracolumbar level is due to irregular growth and deficiency of the superior half of the vertebral bodies. This is occasionally associated with slipping and a gibbus deformity.

The skull is unusual in configuration with a circumference that is always greater than normal. The dolichocephalic type of skull predominates although other types have been noted. Prominence of the frontal bones with heavy supraorbital

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ridges is a common finding. The sella turcica is elongated and shallow with a long anterior recess extending beneath the anterior clinoid processes—the so-called "J" shaped sella. The mandible is frequently broad and heavy with the teeth widely spaced, irregular and poorly developed. In addition, we have recently observed an abnormality of the mandibular condyle which appears to be specific for gargoylism and has prompted us to review the skull roentgenograms in this unusual disorder.

MATERIAL AND RESULTS

The skull roentgenograms of the last 20 patients with gargoylism seen at the Babies Hospital were reviewed to determine the specificity of the condylar change to be described and to document the nature of the usual skull changes associated with this syndrome. The age of the patients at the time of examination ranged from two months to twelve years with the majority being in the two to six year age group. There were 13 males and 7 females. All patients fulfilled the criteria of gargoylism on clinical and roentgenologic grounds and those tested were found to excrete excessive quantities of chondroitin and heparitin sulfate in the urine. The quantity excreted did not correlate with the severity of the clinical or roentgenologic manifestations. The skeletal changes ranged from minimal to the classic far advanced changes.

All types of skull configurations were encountered in this group, but the most common was the dolichocephalic type (Fig. 1, *A* and *B*). Prominent interdigitations along the coronal suture were observed frequently and appeared to be related to the age of the patient at the time of examination. With the exception of one patient who was eight years old, all examples of prominent interdigitations were noted in the two to three year age group (Fig. 2).

The sella turcica in all instances was elongated and shallow with a long anterior recess extending beneath the anterior clinoid processes (Fig. 3). This is the so-called "J" shaped sella which is nonspecific and can occur as a normal variant as well as in other disease states.

Prominent supraorbital ridges with associated depression of the bridge of the nose were noted in 8 patients. The orbits in all

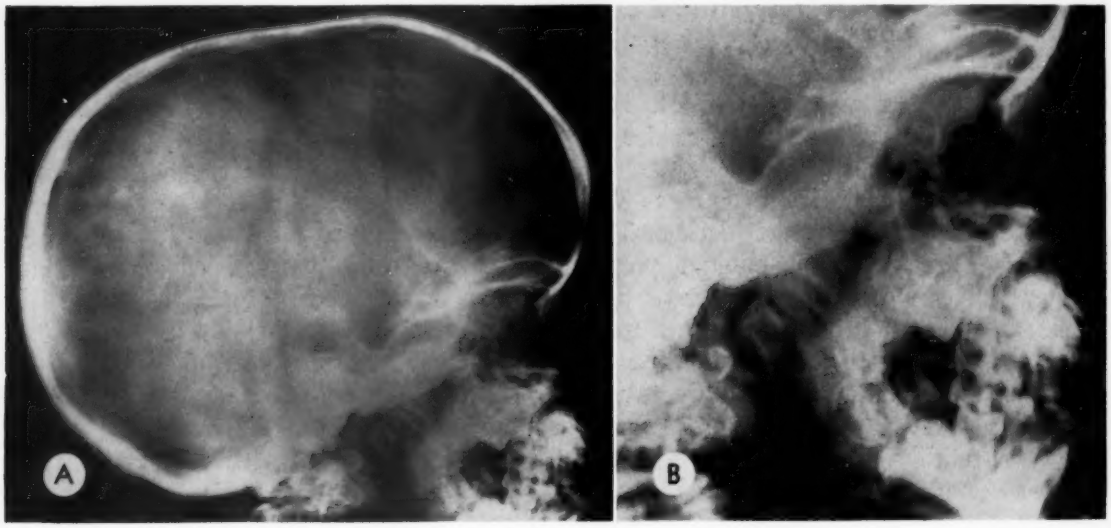

FIG. 1. (*A*) U915474 Four year old white male with typical clinical and roentgenographic features of gargoylism. The lateral roentgenogram of the skull demonstrates the long anteroposterior dimension, the "J" shaped sella turcica and the flat, slightly concave condylar surface of the mandible. (*B*) The flattened and slightly concave articular surface of the mandibular condyle is demonstrated to better advantage.

patients studied were of normal configuration. Special studies of the optic foramina were not available for review. Sinus development was markedly retarded with absence of the frontal sinus noted in every patient. Likewise, mastoid development was poor and lack of pneumatization of the sphenoid sinus was a constant finding.

The mandible presented a rather characteristic appearance on the frontal roentgenogram (Fig. 4). It was short and broad with a resultant square configuration. This appearance was found in 75 per cent of the patients studied. Dentition was also abnormal with the teeth irregularly spaced and poorly developed. Despite these abnormalities, no complaints referable to difficulty in mastication were noted.

The condyle of the mandible was observed to have either of two characteristic appearances. In the patients with marked skeletal changes, the condyle had a concave superior surface (Fig. 1, *A* and *B*, 3, and 5) while in those patients with less marked skeletal disease, the condyle presented a flattened articular surface (Fig. 6). This was noted in 12 of 15 patients where the condyles could be satisfactorily visualized on the lateral skull roentgenograms. In order to determine whether the abnormal appearance of the mandibular condyle was merely fortuitous, the skull roentgenograms of a group of patients with achondroplasia, Morquio's disease, and abnormal skull configurations were reviewed. In no instance was a similar appearance of the mandibular condyle noted. Thus, this condylar configuration may be specific for gargoylism.

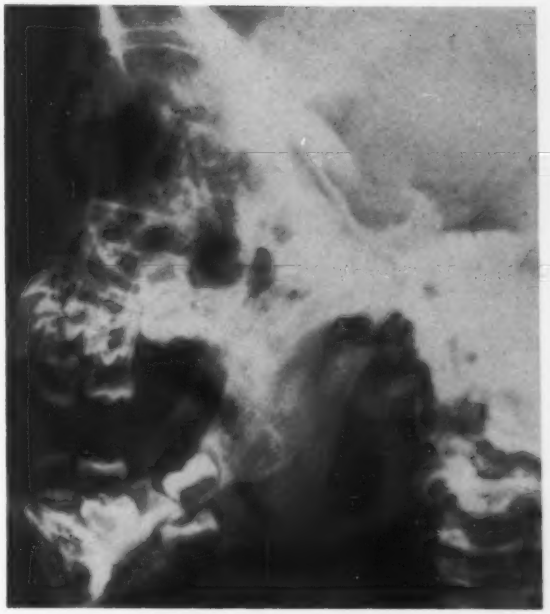

Fig. 3. U1368447 Four year old white female with typical skeletal features of gargoylism and positive urinary chondroitin test. The lateral roentgenogram of the skull shows the elongated "J" shaped sella turcica and the concave superior articular surface of the mandibular condyle.

Fig. 2. U1376758 Two year old Negro male with typical features of gargoylism. Note the prominent interdigital markings along the coronal suture as well as the elongated sella turcica.

DISCUSSION

The condylar abnormality in gargoylism has been alluded to previously in the literature, but to our knowledge has never been illustrated and described prior to this re

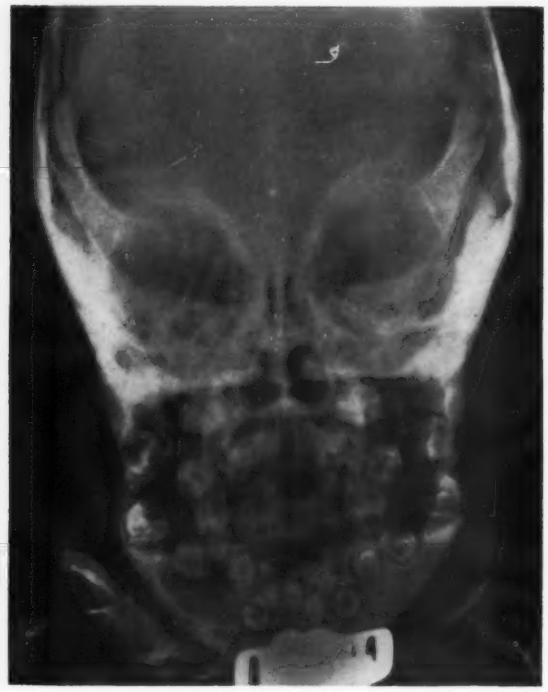

FIG. 4. U1442036 Eight year old while male with typical and severe changes of gargoylism as well as a positive urinary chondroitin test. The frontal roentgenogram of the skull demonstrates the "square," broad appearance of the mandible. Note also the abnormal dentition and poor sinus development.

port. Jervis,[9] in describing the skeletal changes associated with gargoylism, stated that there were "poorly formed articulating surfaces observed at best in the mandibular fossa and the acetabula." However, the appearance of the condyles was not illustrated or described in further detail and no reference was made to the specificity of the change. Lindsay and coworkers'[11] Case 2 is stated to have had rudimentary condyles, but no illustration or additional description of the condylar abnormality was presented. Pendergrass *et al.*[13] state that the ascending mandibular rami are underdeveloped, but no specific alteration of the mandibular condyles is mentioned. In Harvey's[4] report Figure 2 of the skull demonstrates the condylar change, but no comment regarding this abnormality is made in his otherwise excellent description of the skull changes associated with gargoylism.

The roentgenographic appearance of the mandibular condyles in older patients is unknown since longitudinal studies of these patients were not available. However, this abnormality probably persists into adult life in those patients who survive, as evidenced by illustrations in several other publications.[1,2]

On many occasions there is overlap roentgenologically between the various skeletal dystrophies and this makes their differentiation difficult. This is especially true with respect to gargoylism and Morquio's disease. In milder cases the skeletal changes may be similar and impossible to differentiate. However, the condylar configuration occurring in gargoylism in our experience has been a specific finding and, when present, permits a definite diagnosis.

Smith *et al.*[15] state that gargoylism "presents diagnostic roentgenographic features, particularly in the skull." This opinion was based primarily on the configuration of the sella turcica which has been shown to be a nonspecific although constant finding in

FIG. 5. U1441480 Nine year old white male with characteristic facies and skeletal features of gargoylism. The lateral roentgenogram shows the concave articular surface of the mandibular condyle.

gargoylism. On the other hand, we would agree with their statement, but on different grounds. The patient with classic clinical and roentgenographic features of gargoylism will present diagnostic changes in the skull also. These changes consist of dolichocephaly, prominent interdigitations along the coronal suture, elongation of the sella turcica with a long anterior recess beneath the anterior clinoid processes, prominent supraorbital ridges with depression of the bridge of the nose, retardation of sinus development with failure of development of the frontal sinus, square configuration of the mandible and a flattened or concave superior surface of the mandibular condyle. All of these findings, however, are nonspecific with the exception of the last. It should be stated that this abnormality, like the other skeletal features, develops after the first year of life and has not been seen in any patient younger than one year.

Fig. 6. U296608 Two year old white female with mild clinical and roentgenographic manifestations of gargoylism. The lateral roentgenogram of the skull demonstrates slight flattening of the mandibular condyle.

SUMMARY

1. The skull roentgenograms of 20 patients with gargoylism have been reviewed and a new finding has been described.

2. Concavity or flattening of the articular surface of the mandibular condyle has been observed to be a specific finding.

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ILIAC HORNS: A PATHOGNOMONIC ROENTGEN SIGN OF FAMILIAL ONYCHO-OSTEODYSPLASIA*

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HORN-LIKE osseous protrusions from the iliac bones are seldom encountered in daily radiologic practice. Even when these "iliac horns" are noted, their specific diagnostic significance may not be appreciated. It is the author's purpose to present examples of this entity and to pathognomonically relate it to an unusual familial onycho-osteodysplasia.

ILLIAC HORNS

Iliac horns are bilateral, not necessarily symmetric, osseous prominences which protrude posteriorly and laterally from the dorsal aspects of human iliac bones (Fig. 1 and 2). They are not known to occur in other mammals or lower forms.[5] These horns may be clinically palpable and their variable size is not related to the age or sex of the patients in whom they have been described. In many of the younger individuals, epiphyses may be seen capping the structures (Fig. 5 and 6). Opacification of pelvic muscle planes with injected contrast medium[2] suggests that these horns are not located at the origin or insertion of regional musculature, as is the case with osteocartilaginous exostoses.

It is striking that the reported patients with iliac horns have had associated characteristic bone or nail abnormalities or both. Further, the reported individuals belonged to families containing members with similar changes. Two recently observed illustrative cases are described.

REPORT OF CASES

CASE 1. A forty-one year old white female presented with a history of lower abdominal pain of two days' duration. This subsequently disappeared and the patient has been well since.

FIG. 1. Case 1. Note the slightly asymmetric "iliac horns." Also present are iliac bone hypoplasia, coxa valga and supra-acetabular notching

There was no history of previous major illness.

Because of pelvic findings on the abdominal roentgenogram the patient was recalled and the following physical findings, present since birth, were noted: (a) fingernail dystrophy (Fig. 3), most marked in the thumbnails but involving the other fingers and sparing the toenails; (b) bony prominences of both elbows with partial limitation of extension and flexion; and (c) palpable prominences in the region of the buttocks.

Roentgen Findings. Roentgenograms of the abdomen and pelvis revealed bilateral iliac bone protrusions which projected posteriorly in the oblique views. Unusual flattening of the outer aspects of the iliac bones was noted as well as supra-acetabular notching and coxa valga hip deformities (Fig. 1 and 2). Roentgenograms of the elbows (Fig. 4) revealed marked bilateral humeral capitulum underdevelopment and radial head luxation. Some hyperplasia of the olecranon process was present. Roentgen studies of the chest, knees and ankles were normal. Roentgenography of the hands revealed a stubby appearance of the ulna and radial styloids.

* This material has been reviewed by the Office of The Surgeon General, Department of the Army, and there is no objection to its presentation and/or publication if this review does not imply any indorsement of the opinions advanced or any recommendation of such products as may be named.

Comment. The patient's two younger daughters were subsequently examined and no abnormalities were found. (Her oldest daughter is described below.) There are no known similar abnormalities in the patient's parents, grandparents and siblings. Her husband was not available for examination but has no known nail or bone abnormalities.

Case II. This patient is a healthy thirteen year old white female, the oldest daughter of Case I, who was examined after her mother's findings were noted. Present since birth were the following physical findings: (a) fingernail dystrophy (Fig. 7), most severely affecting the thumbs with lesser involvement of the index fingers and sparing the toenails; and (b) partial limitation of elbow extension and flexion.

Roentgen Findings. Roentgenograms of the pelvis revealed bilateral small iliac horns capped by ununited epiphyses (Fig. 5 and 6). Supra-acetabular notching, flattening of the iliac bones and bilateral coxa valga hip deformities were present, changes similar to those of the mother. Roentgen studies of the elbows revealed humeral capitulum hypoplasia and radial head hyperplasia (Fig. 8). Roentgenograms of the chest, hands, knees and ankles were normal.

Fig. 2. Case I. An oblique view reveals the right-sided bony prominence projecting posteriolaterally. Similar findings are present on the left.

DISCUSSION

In our material, as with previously reported cases, iliac horns were discovered either as an accidental finding in a patient with unrelated complaints or at the subsequent examination of asymptomatic relatives.

CLASSIFICATION OF THE CHANGES

Three general groups of changes have been associated with iliac horns: (A) nail

Fig. 3. Case I. Marked thumbnail dystrophy with lesser involvement of the index fingers, ring fingers and little fingers.

FIG. 4. Case 1. Right elbow. Hypoplasia of the capitulum humeri and hyperplasia of the medial epicondyle, with luxation and hyperplasia of the radial head.

dystrophies, (B) bone dysplasias, and (C) miscellaneous abnormalities.

A. *Nail Dystrophies.* The thumbnails often present with small normal bases which thin and tend to disappear distally,

FIG. 5. Case II. Note the small bilateral "iliac horns," partially obscured by bowel on the left. Also present are iliac bone hypoplasia, coxa valga and supra-acetabular notching.

FIG. 6. Case II. Close-up of the right ilium revealing a small iliac horn capped by epiphysis. There was a similar finding on the left side.

merging with the fleshy tips of the fingers so that there are no free ends of the nails. Other fingernails and the toenails are less often involved and may be marred by longitudinal ridges and lateral concavities (Fig. 3 and 7).

B. *Bone Dysplasias.* The involved osseous structures present with various hypoplasias or hyperplasias. Elbow and knee joint bones are most commonly involved. The capitulum humeri is hypoplastic (Fig. 4 and 8) and there is a tendency to radial head luxation, hypoplasia or hyperplasia. Hyperplasia of the coronoid process of the ulna and of the medial epicondyle of the humerus may occur. Variable degrees of limitation of elbow flexion and extension are common. Agenesis or hypoplasia of the patella is often present with a tendency to habitual dislocation. There may be hyperplasia of the femoral condyle and continuous hypoplasia of the tibial plateau. Although knee abnormalities are commonly seen, they were not present in our cases.

In addition to iliac horns, the pelvis may present with any or all of the following: hypoplastic iliac wings, supra-acetabular notching, protrusio acetabuli and coxa valga. Other minor periarticular hypoplasias or hyperplasias have been reported and are summarized elsewhere.[8]

C. *Miscellaneous Abnormalities.* An irregular zone of pigmentation separating the

Fig. 7. Case II. Marked thumbnail dystrophy with lesser involvement of the index fingers.

pupil from the iris is uncommonly associated with iliac horns.[6,10] "Hereditary glomerulonephritis" has been reported in a family with iliac horns and the above changes.[5] In 1 reported case, nonunion of a simple forearm fracture was considered a manifestation of generalized bone abnormality.[8]

All or some of the above general groups of changes have been found in patients with iliac horns and in their families. Generally, no significant incapacity is associated, although some did have osteoarthritides, which may have been secondary to the periarticular dysplasias. It should be noted that the nail and bone changes commonly occur in relatives of the reported cases, even though iliac horns are absent.

REPORTS IN THE LITERATURE

As a matter of interest, an unusual familial entity characterized by all or some of the knee and elbow dysplasias and nail dystrophies has been known since the last century[7] and has been repeatedly described.[8] Of radiologic significance is the fact that Turner,[14] in reporting two families with these changes, included a pelvic roentgenogram clearly showing iliac horns. He, however, made no mention of this finding. Lester,[6] reported another family and mentions, without illustrative studies, that the "crest of the ilium seems enlarged posteriorly." Fong[4] briefly described a patient with iliac horns but apparently little clinical information was available to him.

Mino, Mino, and Livingstone[9] were the

Fig. 8. Case II. Right elbow. Hypoplasia of the capitulum humeri and hyperplasia of the radial head.

first to relate iliac horns to the previously known onycho-osteodysplasia. Since then, iliac horns have been described by Thompson, Walker and Weens,[12] Hawkins and Smith,[5] Böck,[2] Roeckerath,[10] Cottet and Pfändler,[3] Wedler and Welsch,[15] Bates,[1] Toison, Guillemet and Carlier,[13] and by Mangini[8] in 36 individuals, whose ages have ranged from nine months to sixty-five years. In no case has the observation of iliac horns been an isolated finding and either one or more manifestations of onycho-osteodysplasia have been associated.

GENETICS

The hereditary mechanism involved in these unusual ectodermal and mesodermal abnormalities is far from clear.

One hypothesis[11] implicates a single polyphenotypic dominant nonsex-linked gene which is able to cause many deformities in varying degrees. Such a mechanism is the generally accepted one in other abnormalities, *e.g.*, osteogenesis imperfecta. Another theory[10] suggests that partial or complete manifestations of the complex are best explained by many genes on one chromosome with the resultant effect dependent upon their closeness. Some even deny a hereditary mechanism and suggest alterations in the maternal biochemical or physiologic milieu. Supporting this opinion is the ability of investigators to consistently obtain skeletal and soft tissue anomalies in the offspring of female rats maintained on riboflavin deficient diets.[9] Still another point of view[8] maintains that two pathologic genes are present, one determining nail dystrophy and the other influencing arthrodysplasia, but that their net effect is influenced by interactions with several environmental factors, such as metabolic errors and accidents. The result is that some family members do not have stigmata of the disease while others have varying manifestations.

Chondroectodermal dysplasia (Ellis—Van Crevald) can also involve nails and bony structures such as the pelvis and elbows. However, the absence of knee changes or familial incidence and the marked dentition abnormality indicate an unrelated entity.

SUMMARY

Iliac horns are a pathognomonic roentgen sign of familial onycho-osteodysplasia. Their discovery should alert the radiologist to initiate a search for characteristic unguinal and osseous changes in the patient and his family.

Two related cases with iliac horns and onycho-osteodysplasia are presented.

The literature is reviewed and possible genetic mechanisms are discussed.

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ROENTGENOLOGIC ASPECTS OF HIP LIMP IN CHILDHOOD*

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THE problem of hip limp in childhood is one which is encountered by the general practitioner, pediatrician and orthopedist as well as the radiologist. The causes of limp are numerous, ranging from such diverse conditions as improperly fitting shoes and behavior problems to disorders that produce permanent crippling if not treated early and adequately.

The purpose of this paper is not to present an exhaustive list of everything which might produce limp, or to demonstrate roentgen findings in gross, far advanced cases, but rather to emphasize the early and minimal findings. Limp due to neurogenic causes is not included in the discussion.

The abnormalities found in the growing hip constitute an interesting group of conditions which commonly present themselves as limp, either painful or painless, or as pain referred to the knee or anterior thigh. Early diagnosis is important in all of these ailments, and in some of them it is critical.

Roentgenograms of high quality, showing both bone and soft tissue detail, are essential. Both hips (in anteroposterior and lateral projection) should be routinely examined. This is because of the frequency of bilateral involvement and the desirability of comparing sides as an aid in detecting minimal changes. Taking an anteroposterior roentgenogram of the pelvis, to include both hips, and a lateral roentgenogram of the hips in "frog leg" position is a good routine practice.

These conditions are presented in the order in which they are usually seen, starting with the defects found in younger patients and progressing to those in older patients.

CONGENITAL DISLOCATION OF THE HIP

Ideally, congenital dislocation of the hip should not be included in the causes of hip limp in childhood. It should be diagnosed by physical examination shortly after birth; a diagnosis made after the child has started to walk is a late diagnosis.[6] Bilateral congenital dislocation of the hip is more difficult to diagnose clinically than the unilateral cases because the abnormal findings are symmetric and more easily overlooked.

On examination, the skin folds are seen to be asymmetric, the infant is reluctant to use the affected extremity and there is shortening of the involved extremity. When the patient lies flat on his back with both hips and knees flexed, the affected leg appears shorter and will resist full abduction. After the child begins to walk, there is a painless limp in unilateral cases. In bilateral cases the gait is said to be typical and is waddling in type. There is a prominent abdomen and increased lumbar lordosis since the line of weight-bearing is shifted posterior to the acetabulum.

Congenital dislocation of the hip is approximately six times more common in female than in male infants. It is more often unilateral, and is very rare in Negro infants. In Asiatic countries, where the child is carried on the mother's hip, with the legs abducted, the incidence of congenital dislocation is reduced.[3]

On roentgen examination, before the appearance of the capital femoral epiphysis, the increased slant of the acetabular roof may be the only abnormal finding; displacement of the femoral shaft upward and laterally may also be noted. Interpretation of the former finding is difficult, since increased slant of the acetabular roof does

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not always mean that the child has or will develop congenital dislocation of the hip.[1]

After the appearance of the capital femoral epiphysis, usually at about the age of six months, recognition is easier. In congenital dislocation there may be delay in the appearance of the capital femoral epiphysis and, once it appears, it may be smaller than normal. Comparison with the opposite side is helpful.

The radiologist should consider the possibility of congenital dislocation in cases of increased slope of the acetabular roof, lateral and upward displacement of the femoral shaft, or asymmetric or underdevelopment of the capital femoral epiphysis. These suggestive roentgen findings, when correlated with the physical findings, offer the optimum chance for early diagnosis (Fig. 1).

FIG. 1. Congenital dislocation of the right hip. Neither capital femoral epiphysis has appeared. There is increased slope of the right acetabulum and displacement of the femoral shaft laterally and cephalad.

COXA VARA

This term refers to a condition in which there is a decrease in angulation between the femoral neck and shaft. Normally, the angle of the femoral neck is 120–130 degrees, but in coxa vara it may be 60 degrees or less. The defect may be congenital or acquired. Very little is known of the pathology of the congenital type. It is assumed to be due to anomalous ossification of the proximal third of the femur. Acquired types may be associated with rickets, osteomalacia and fractures of the femoral neck (either traumatic or pathologic) and other causes.

The limp associated with coxa vara is painless. It may appear in children learning to walk, or it may have an insidious onset in later years following minor trauma.

The physical examination shows limitation of abduction and internal rotation. In bilateral cases, as with congenital dislocation, there is increased lumbar lordosis and a protuberant abdomen. The femoral head is palpable, however, in its normal location and there is no telescoping. Clinically, coxa vara is similar to congenital dislocation except for these latter two findings.

This condition is usually easy to diagnose on roentgen examination, which shows the decreased angulation between the femoral neck and shaft as described. If the condition is acquired, or associated with another disease, other stigmata may be seen on the roentgenograms of the pelvis or other parts (Fig. 2).

PYOGENIC INFECTION OF THE HIP

This condition may appear a few days following birth and most cases are observed in infants. It does not commonly produce limp, since the child is usually too ill or too young to walk. If the hip joint is to be saved, prompt diagnosis is essential. There is early destruction of the joint cartilage by proteolytic enzymes produced by the pyogenic organisms. It may start as an osteomyelitis of the femoral neck and, because the femoral neck is contained within the joint capsule, spread to the joint itself.

The patients usually appear acutely ill, but not invariably so. There is marked

FIG. 2. Congenital bilateral coxa vara. There is a marked decrease in the angle between the femoral shaft and neck. This is a typical finding and usually makes possible an easy roentgen diagnosis.

limitation of motion, fullness about the hip joint, fever and leukocytosis. This condition usually presents an acute fulminating picture as opposed to tuberculosis of the hip, which is usually insidious and not common in such young infants. The hip infection may be secondary to infection elsewhere, as in the urinary tract, respiratory tract or skin. However, it may also be primary within the hip itself.

On roentgen examination there is widening of the joint space and prominence of the shadow of the joint capsule. Areas of destruction in the femoral neck may appear later. Destruction may be greater in degree than it appears on the roentgenogram because so much of the femoral head and neck is cartilage in infants.[3] In advanced cases actual dislocation of the joint may occur.

TUBERCULOSIS OF THE HIP

The hip is the most common joint involved by tuberculosis and constitutes 20 per cent of cases of bone and joint tuberculosis.[3]

The tubercle bacillus reaches the joint by hematogenous spread and may primarily involve the synovia or inferior neck adjacent to the epiphyseal line, but it is best to consider it as a general involvement of the joint.

The condition has an insidious onset with hip pain, limp, atrophy of leg muscles, afternoon fever and, frequently, night cries. As in most causes of childhood limp, the pain may be referred to the knee or thigh with little or no complaint of hip pain. Pain is often worse on arising but improving with activity, only to recur following longer periods of exercise. If untreated, after weeks or months activity becomes impossible and the patient is bedridden.

The tuberculin test is practically always positive and a negative tuberculin test with a suspected tuberculous hip should lead to checking of the antigen and use of another source.[3] Tuberculous infection of the hip is infrequent under two years of age.

On early roentgen examination, there is widening of the joint space due to increased joint fluid and decreased density of the bones of the hip, extending into the proximal portions of the neck of the femur. Later, the joint space is narrowed. Although there are no proteolytic enzymes associated with tuberculous infection, progression of the disease is so slow that the narrowing of the joint space stands out. There is prominence of the capsular shadow; trabeculae become less prominent and have a hazy appearance. The disease may progress to gross bone destruction (Fig. 3).

SYNOVITIS OF THE HIP

This is a very important and probably the most common cause of hip limp in childhood. It bears a poorly understood relationship to other more serious hip diseases in children and adults. Children with synovitis of the hip have an increased probability of developing Legg-Perthes' disease and synovitis appears at times to be the first symptom of an incipient form of the disease. It may be an underlying cause in any unilateral degenerative hip disease discovered in the second decade of life.

The etiology is unknown. Trauma, allergy, and toxic factors have been postulated, but none of these factors can apply to all cases.[2]

Clinically, the condition closely mimics Legg-Perthes' disease. The limp, age group and physical findings are very similar.

It has been called the most common cause of irritable hip in the older child with a negative roentgen examination.[5] A close study of good quality roentgenograms, however, will reveal positive findings. The soft tissue shadow of the joint capsule is thickened and bulges laterally and superiorly. Comparison with the opposite side is helpful. Soft tissue swelling of muscles (obturator internus, gluteus minimus and iliopsoas) is a less constant finding and more difficult to interpret. There may also be slight widening of the joint space due to an increase in fluid. This is more easily detected medially[2] (Fig. 4).

The symptoms usually subside rapidly with treatment and this also aids in differentiating synovitis from other clinically similar hip conditions.

Fig. 4. Synovitis of the right hip. There is marked lateral bulging of the capsule of the right hip. The capsule of the left hip joint appears normal.

Legg-Perthes' disease

This is a common and serious cause of hip limp in children. It is the most common of the osteochondroses. It occurs primarily in a four to twelve year age group.

Fig. 3. Tuberculosis of the left hip. There is widening of the joint space medially and widening of the epiphyseal line. An ill-defined area of destruction is noted in the femoral neck. At surgery a reddish-brown fluid spurted out when the capsule was opened. Culture revealed tubercle bacillus.

Like in other types of osteochondrosis, the basis for this disease appears to be circulatory impairment of the growing bone. There is involvement of the capital femoral epiphysis with sequestration of this area followed by gradual regrowth over a period of years. The condition is approximately 8 to 1 times more common in males, suggesting that physical activity may have some relation to the cause.

It is important to examine both hips because of the frequency of bilateral involvement. If, initially, the disease is unilateral, the opposite hip should be observed at intervals during treatment for possible beginning involvement. As mentioned above, there is sometimes preceding or associated synovitis. Cases observed at surgery have shown evidence of synovitis.

Clinically there is a history of limp, with pain at the knee or hip, for a period of three weeks to two months. There may be atrophy of the thigh muscles on the involved side. Symptoms are not always present from the beginning of the disease. Some cases are seen with a short duration of symptoms and advanced roentgen changes. The insidious onset sometimes simulates

FIG. 5. Legg-Perthes' disease of the right hip. There is slight rarefaction of the right femoral neck and minimal widening of the epiphyseal line with some irregularity and flattening of the right capital femoral epiphysis.

tuberculosis of the hip as well as other chronic hip lesions.

The earliest roentgen sign is widening of the epiphyseal line and irregularity of the metaphysis of the femoral neck. The articular capsule may be prominent. Rarefaction of the femoral neck occurs. Later there is flattening of the femoral head with the neck becoming short and thick, and the capital femoral epiphysis has a sclerotic, fragmented appearance (Fig. 5).

SLIPPED CAPITAL FEMORAL EPIPHYSIS

This condition occurs in a slightly older age group (nine to sixteen years); *i.e.*, preadolescent and adolescent children. It is commonly seen in obese and poorly developed children, although tall asthenic children may also develop slipping of this epiphysis.

The plane of the epiphyseal line changes from the horizontal to the oblique as the child becomes adolescent and it has been postulated that this makes the epiphysis vulnerable to a shearing force from the increased angulation.[1] This produces a chronic limp, which may or may not be painful. The pain is frequently referred to the knee. Clinically the limp shows little difference from the limp of Legg-Perthes' disease.

The early roentgen findings are similar to those in Legg-Perthes' disease, namely, widening of the epiphyseal line and rarefaction of the femoral neck. The slipping usually is downward and backward from the normal position, or it may also be medial. Klein *et al.*[4] have stated that a line drawn along the superior border of the femoral neck, on the anteroposterior roentgenogram, should transect the capital femoral epiphysis (Fig. 6). In cases of medial slipping this transection would not occur. Without attention to this detail, medial slipping could easily be overlooked. Posterior slipping is detected in the lateral view which usually demonstrates an obvious change in the relationship between the epiphysis and the femoral neck.

SUMMARY

1. Good quality roentgenograms and attention to minimal findings are necessary for early diagnosis of conditions causing hip limp in childhood.

2. Comparison with the opposite side is helpful in detecting early changes.

3. Early diagnosis is important in all

FIG. 6. Slipping of the left capital femoral epiphysis. Slight medial slipping on the left is noted; a line drawn along the superior border of the femoral neck would not transect the epiphysis, as it would on the right.

these conditions, and critical in some; any help the radiologist can give the clinician will increase the chance of earlier recognition.

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BILATERAL INCURVING OF THE TERMINAL PHALANGES OF THE FIFTH FINGERS*

AN ISOLATED LESION OF THE EPIPHYSEAL PLATE

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CONGENITAL anomalies involving the phalanges are, on the whole, easily recognized and classified. Particularly, the incurving of the fifth finger is well known as a stigma of mongolism or as an isolated anomaly occurring sometimes as a familial trait. There also exists, however, a condition of apparently acquired nature affecting the terminal phalanx of the fifth finger.

Kirner[3] is credited with the first description, in 1927, of this disorder. A few subsequent publications have been devoted to this entity, bringing the total number of cases reported so far to 14.[1,2,4–9] From the data available in these reports it appears justified to delineate this disorder in a clear fashion from all the other affections involving the phalanges of the fifth fingers. Since, in the American literature, there is no information available on this peculiar bony disturbance, we would like to report the findings of a case recently seen at the Children's Hospital of Basel, Switzerland, together with the data of a second case from the files of the X-ray Department of the Children's Hospital, Boston, Massachusetts.

CLINICAL FEATURES

From the accumulated data it can be seen that this disorder is first noticed in preadolescence, between the ages of eight and fourteen years. Girls appear to be affected more frequently than boys, in a ratio of about 2:1. According to the histories, trauma does not seem to play any role.

The onset is insidious with the parents usually reporting slow deviation of the terminal phalanx of the little fingers manifesting itself in a progressive manner over a period of many months or even years. There are no subjective complaints of pain or neurologic manifestations. The only difficulty a patient may encounter is in the execution of skilled acts requiring the use of the little fingers, such as, playing the violin or piano, or using a typewriter.

Objectively, there is usually minimal redness over the affected phalanx with some degree of swelling. However, no tenderness or hyperthermia can be noticed. In no instance were there signs of local infection. The position of the axis of the terminal phalanx of the fifth fingers is strikingly and uniformly abnormal. There is a considerable degree of palmar and radial deviation with an element of rotation (supination) of the most distal portion of the fifth fingers. The convexity of the fingernails may be abnormally pronounced.

ROENTGEN FEATURES

The deviation, as seen on the roentgenogram, does not affect the entire terminal phalanx but only its diaphysis. The epiphysis is in the normal position. The joint space between the middle and terminal phalanx is normally preserved. The metaphysis is ill defined, if visualized at all. In some cases, the epiphyses appear thicker than those of the unaffected terminal phalanges or fingers. The space of the epiphyseal plate is generally widened. The diaphysis deviates 10° to 50° radially from its normal axis and to almost the same degree in the palmar direction. The diaphyses are markedly narrowed; they

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appear bent and show a loss of normal trabeculation. The cortical portions are often ill defined with an irregular contour, particularly on the palmar and radial sides. These changes can be present in varying degrees according to the stage of the disease process.

REPORT OF CASES

Case 1. This nine year old girl was seen at the Children's Hospital of the University of Basel. At the time of admission to the hospital for a diagnostic work-up for an unrelated disorder, it was noted that the terminal phalanges of the fifth fingers deviated symmetrically in a palmar and radial direction. She was the only child of healthy parents and there was no information available on any bony abnormalities in the father's or mother's families. The parents claimed that the abnormal shape and direction of the tips of both fifth fingers had been present for some time (several years?) but that the changes observed in early infancy were by no means as marked as at the present. At no time were there subjective complaints. Trauma of any kind was denied.

Fig. 1. Case 1. Dorsal view showing the incurved terminal phalanges of the fifth fingers. The swelling over the distal phalangeal joints is well visualized.

Physical Examination. Both terminal phalanges of the fifth fingers deviated radially by 40° to 50° (Fig. 1) and to a similar degree in the palmar direction when viewed in the lateral aspect. In the region of the distal joints of both the affected fingers, there was a mild degree of diffuse swelling and thickening of the skin together with minimal redness, but no local hyperthermia or pain to pressure. Skin sensitiv-

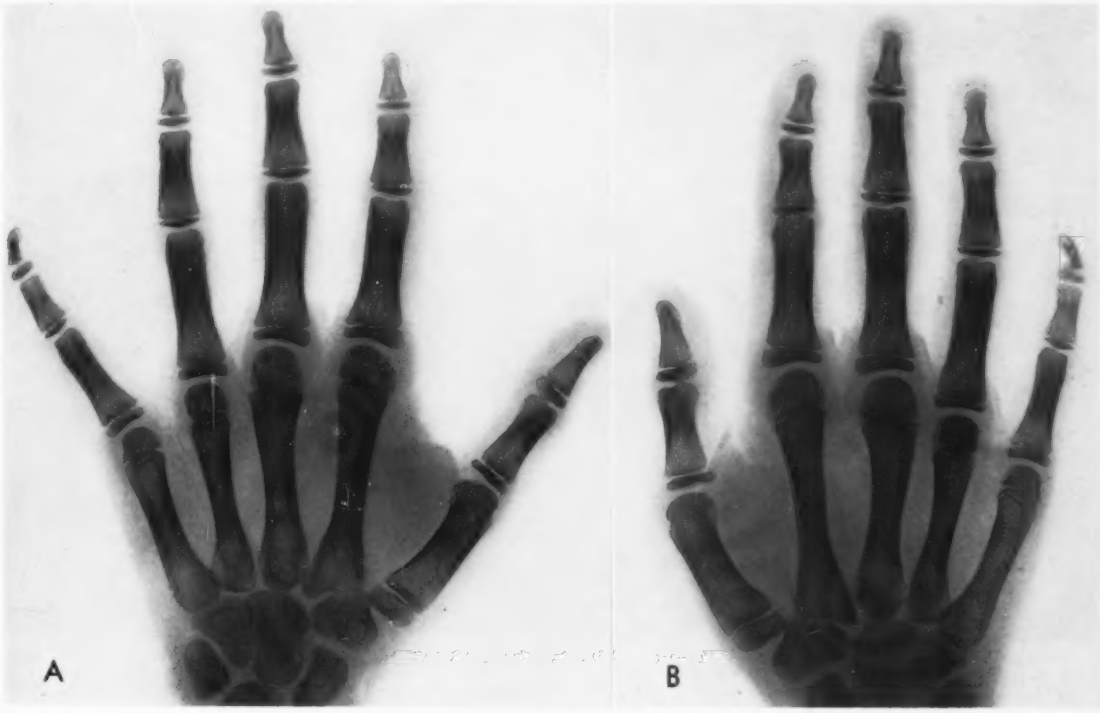

Fig. 2. Case 1. (*A* and *B*) Posteroanterior roentgenograms of both hands.

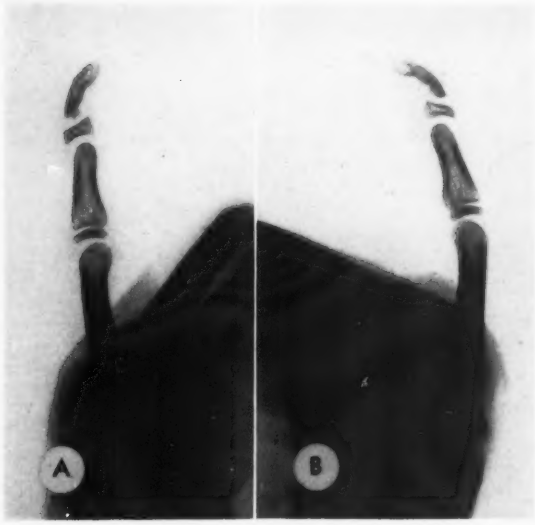

FIG. 3. Case I. (*A* and *B*) Lateral roentgenograms of the fifth finger of each hand.

ity and proprioception were normal. The range of motion of the joint was only mildly restricted in that neither complete extension nor complete flexion could be achieved.

Roentgen Findings. The only abnormal findings are limited symmetrically to both terminal phalanges of the fifth fingers (Fig. 2, *A* and *B*; and 3, *A* and *B*). The diaphysis is in an abnormal relationship to the epiphysis with widening of the epiphyseal plate. The trabeculation of the diaphysis is highly irregular with areas of increased density in the central portions and less definition of the cortex, particularly on the palmar and radial sides. Also there is marked structural loss of the metaphysis. No signs of osteolysis, bony sequestration or callus formation can be recognized. A skeletal survey revealed nothing abnormal.

In addition, roentgenograms of the feet of this patient and of the hands and feet of both her mother and father were obtained but they presented no abnormal findings.

CASE II. A ten year old boy was seen at the Children's Hospital, Boston, in the year 1944. He was brought to the hospital for a deformity of both fifth fingers. The mother claimed that during the preceding four years there had been gradual thickening and deviation of the terminal phalanges of the fifth fingers. At no time was there pain, local infection or any joint involvement. According to the history, there had been no significant disease. The boy was fully active with no subjective complaints.

Physical Examination. There was thickening of the terminal phalanges of the fifth fingers with minimal "clubbing" (Fig. 4, *A* and *B*); all other joints were normal. Temperature measurements by skin electrodes revealed no differences between the local affected areas and the rest of the fifth fingers or any portion of the other fingers or their terminal phalanges.

Roentgen Findings. No evident abnormality is present except for that of each fifth finger where there is considerable soft tissue thickening at the tip and considerable deformity of each distal phalanx (Fig. 5, *A*, *B* and *C*). These are irregular in contour, with considerably increased density and palmar and radial devia-

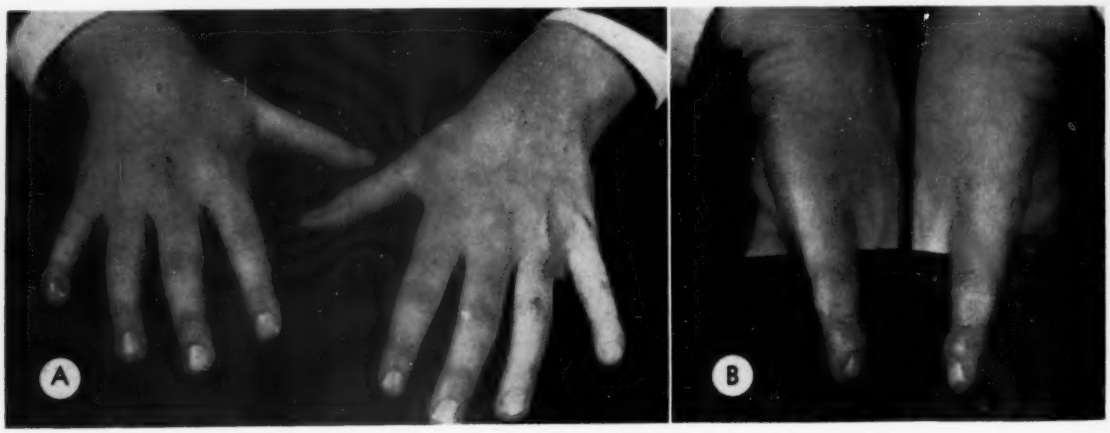

FIG. 4. Case II. (*A*) Photograph of the dorsal aspect of both hands demonstrates the shortness and incurving of the terminal phalanges of the fifth fingers. (*B*) Photograph in the lateral view of the fifth fingers shows the palmar deviation, diffuse swelling over the distal joints and the exaggerated convexity of the fingernails.

Fig. 5. Case II. (*A*) Posteroanterior roentgenogram of both hands. (*B* and *C*) Detailed views of the affected terminal phalanges.

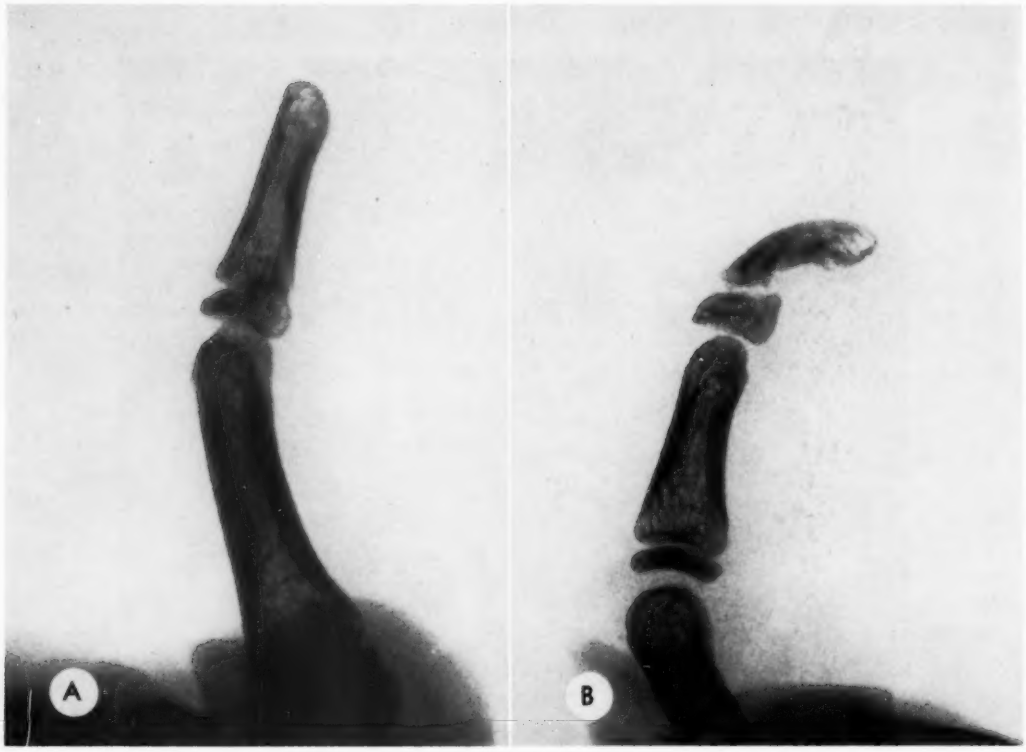

FIG. 6. Case 1. (*A* and *B*) Lateral views of the fourth and fifth fingers.

tion. There is nothing to suggest osteomyelitis. Examination of the long bones revealed no essential variation from the normal.

Comment. The etiology of these changes is not evident but they are such as those frequently associated with a vascular disturbance or conditions such as scleroderma. However, they also may be developmental in nature.

DISCUSSION

From these 2 cases and the 14 other cases recorded to date, the following characteristics of this disorder can be recognized: (1) manifestation between eight and fourteen years of age; (2) painless swelling and progressive palmar and radial deviation of the distal phalanges of the fifth fingers over a period of time (three months to several years); (3) bilateral involvement (in 14 of the 16 patients); (4) usually symmetric progression with, however, single cases showing a slight difference in the stage of the disorder comparing the two sides;[3,6,7] (5) girls affected twice as frequently as boys; (6) normal or slight retardation of closure of the epiphysis but persistent deviation and shortening of the diaphysis of the terminal phalanx with virtual return to normal bony architecture;[5,9] (7) no other pathologic changes of the skeleton; and (8) no familial occurrence.

The question of the nature of this disorder has so far remained open to speculation. In our Case 1 we did a biopsy of one of the affected fingers, at which time it was noted that there was a definite lysis between the diaphysis and epiphysis of the terminal phalanx. The biopsy specimen is presently being reviewed by different authorities on bone pathology and will be reported upon in a later communication.

There appears to be evidence that this is a lesion compatible with aseptic necrosis. The observation of an epiphysiolysis, however, presents a new possibility on the etiology of this rare disorder. In the lateral view of the fourth and fifth fingers of the

left hand in our Case 1 (Fig. 6, *A* and *B*), the separation of the diaphysis is clearly apparent. The epiphysis itself is in a normal position but is markedly thicker than normal. Again, the lack of a well defined metaphysis is noticed, together with the absence of normal trabeculation and poor structural formation of the cortex. We emphasize this point particularly since Schmid[5] proposed the term "juvenile osteomalacia of the terminal phalanx of the small fingers" to describe this disorder. We have not been able to obtain any evidence of an osteomalacic process and feel that this disease primarily affects the formation of the metaphyses of the terminal phalanges of the fifth fingers.

As a secondary mechanism, dominance of the flexor digitorum profundus over the extensor muscles displaces the diaphysis in the described manner. Subsequent to epiphyseal lysis there is a sudden aggravation of the abnormal position of the terminal phalanx. The condition then stabilizes in this abnormal anatomic relationship with ultimate fusion, shortening and retrabeculation of the affected terminal phalanx.

Based on the evidence mentioned and awaiting the outcome of the analyses of the pathologic specimen, we propose, for the time being, to refer to this disorder, using the original descriptive term of Kirner,[3] as "bilateral incurving of the terminal phalanges of the fifth fingers."

SUMMARY

A description of 2 cases of bilateral incurving of the terminal phalanges of the fifth fingers is presented. This rare disorder affects adolescents from eight to fourteen years old, and girls twice as frequently as boys. The finding of a true epiphysiolysis, confirmed at operation, is reported for the first time. Available data on the natural course of this disorder are reviewed. There is ultimate bony union of the slipped elements in their abnormal anatomic relationship. No therapy has been proposed up to the present time.

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SEPARATE CENTERS OF OSSIFICATION OF THE TIP OF THE INTERNAL MALLEOLUS

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SEPARATE centers of ossification of the tip of the internal malleolus have been described by Fairbank,[4] Mouchet,[8] and Den Hoed.[3] Bircher[1] has described an os subtibiale, which is without doubt a nonunion of a separate center of ossification at the tip of the internal malleolus. Mouchet[8] reported the findings in a single child. Lapidus[7] stated in *The Journal of Bone and Joint Surgery*, "Ruckensteiner demonstrated the presence of the distal tibial epiphysis as early as the seventh month of life, in any event nearly always before the second year. According to him, the distal tibial epiphysis develops in transverse direction to the long axis of the limb. As the ossification of the epiphysis reaches the medial lower edge of the tibial diaphysis, the ossification of the epiphysis continues medialward and downward, forming the medial malleolus. The latter takes place only at the age of eight or nine years. At about this time an inconstant independent center of ossification may occasionally be formed at the tip of the medial malleolus. This center seems to unite soon after its appearance. One case was seen by Ruckensteiner." The incidence of this lesion was not specifically investigated by any of the mentioned authors. Den Hoed,[3] in studying the roentgenograms of 150 normal children for ossification development, found 21 cases or 10.7 per cent in which there were separate centers of ossification at the tip of the internal malleolus. Of these, 14 were boys and 7 were girls. He contrasted his findings with those of Fairbank[4] who stated that it occurred more commonly in girls.

Köhler and Zimmer[6] in their book state that the separate center of ossification is common between the ages of eight and nine; however, the incidence, sex distribution or the age of complete ossification of the tibial tip are not given. Caffey[2] states, "In a small percentage of healthy children who have no sign of disease near the ankles, the medial malleolus of the distal epiphyseal cartilage of the tibia will show a separate ossification center . . . the ossicles may be unilateral or bilateral." He does not mention the specific incidence percentage nor sex distribution.

METHODS AND MATERIAL

The Fels longitudinal study is an ideal method by which to determine the time of appearance of extra centers of ossification based on sex. In the past years the character of the population at the Fels Research Institute has not substantially changed. The socioeconomic distribution consists of a group in moderate circumstances, Caucasian in origin and from a background of farmers, tradesmen and people of the middle and lower-middle classes. Many siblings of those in the early study have become part of the present sample. Children born after 1937 and before 1953 constitute the present study group. These children repeatedly underwent complete pediatric examinations. Anthropologic measurements were made of their height, weight, length, chest, skull, and calf. They were examined roentgenographically at birth, at one month, three months, six months, nine months, one year and thereafter at half-yearly intervals until the age of eighteen. The examination usually consisted of roentgenograms of the skull, teeth and of the extremities, including soft tissue roentgenograms of the latter, and of an anteroposterior roentgenogram of the left lower limb which was always available for comparison. A special posture roentgenogram was also taken of children between the ages of two and one-half to eight and one-half years. These included both lower limbs, enabling

one to detect the age at which the extra centers of ossification of the tip of the internal malleolus appeared, whether or not they were bilateral and often when they united with the main mass of the tibia. If the center had not yet appeared, or had not joined the main mass by the age of eight and one-half years, its progress could be traced on the roentgenograms of the left lower limb.

This series consisted of 151 children from 75 families, 88 boys and 63 girls. There were two sets of triplets and three sets of twins. Fifteen of the boys showed roentgenographic evidence of extra ossification centers of the tip of the internal malleolus. The earliest age at which these appeared in the boys was six years, the latest age was eleven. The earliest age at which the centers joined the main mass was six months, the latest twelve years. The boy in whom the ossification center appeared at eleven years and joined at twelve matured slowly (Greulich and Pyle[5]). Of the 63 girls, 30 had extra centers of ossification. Twenty-seven of these had roentgen findings of bilateral centers. Three were found to have extra centers of ossification on the roentgenograms of the left limb since they did not fall in the group which had special posture roentgenograms. The earliest age at which the extra centers appeared in the girls was six and one-half years and the latest age was nine years. The latest age at which the ossification center united with the main mass was eleven and one-half years in a girl in whom the extra tibial center first appeared at nine; she, too, was a late maturer[5] and also a severe asthmatic. The shortest period in which the extra ossification center joined the main mass after its appearance in both girls and boys was six months. Posture roentgenograms taken at eight and one-half years showed that only 4 of the 15 boys had bilateral ossification centers; two were brothers. Table 1 shows the age of appearance and union of the extra centers to the main malleolar mass. The mean age of appearance in girls was 7.65 years; the mean age of union was 8.7 years. The median length of time in which union occurred was 1.14 years. In boys the mean age of appearance was 8.76 years and of union 10.8 years. The median length of time in which union occurred was 1.34 years.

Of the boys, 2 sets of brothers had two extra ossification centers; in the girls 6 sets of sisters had extra centers of ossiffication. One of the group of sisters had a brother who also had an extra center. This was the only family in which the extra centers ap-

TABLE I

AGE OF APPEARANCE OF EXTRA CENTERS

Age (yr.)	6.0	6.5	7.0	7.5	8.0	8.5	9.0	9.5	10.0	10.5	11.0	Combined Total
Boys	1	—	1	1	1	2	5	1	2	—	1	15
Girls	—	6	1	11	3	6	3	—	—	—	—	30
Total	1	6	2	12	4	8	8	1	2	—	1	45

AGE AT WHICH THE EXTRA CENTER JOINED TIBIA

Age (yr.)	6.0	7.5	8.0	8.5	9.0	9.5	10.0	10.5	11.0	11.5	12.0	Combined Total
Boys		1	—	1	1	—	4	—	4	—	1	12
Girls		3	3	10	6	2	4	—	—	1	—	29
Total		4	3	11	7	2	8	—	4	1	1	41

FIG. 1. Female, aged eight years. Roentgenogram shows beginning downgrade of tip.

FIG. 2. Female, aged eight and one-half years. Roentgenogram shows a separate ossification center.

FIG. 3. Female, aged nine years. Roentgenogram shows engulfing of separate ossification center, giving the appearance of an os subtibiale.

FIG. 4. Female, aged eight and one-half years. Roentgenogram shows the downgrowth of the main mass and two separate ossification centers.

Fig. 5. Female, aged nine years. Roentgenogram shows 4 ossification centers outlining the tip.

Fig. 6. Female, aged nine and one-half years. Roentgenogram shows formation of the tip with spherule like areas.

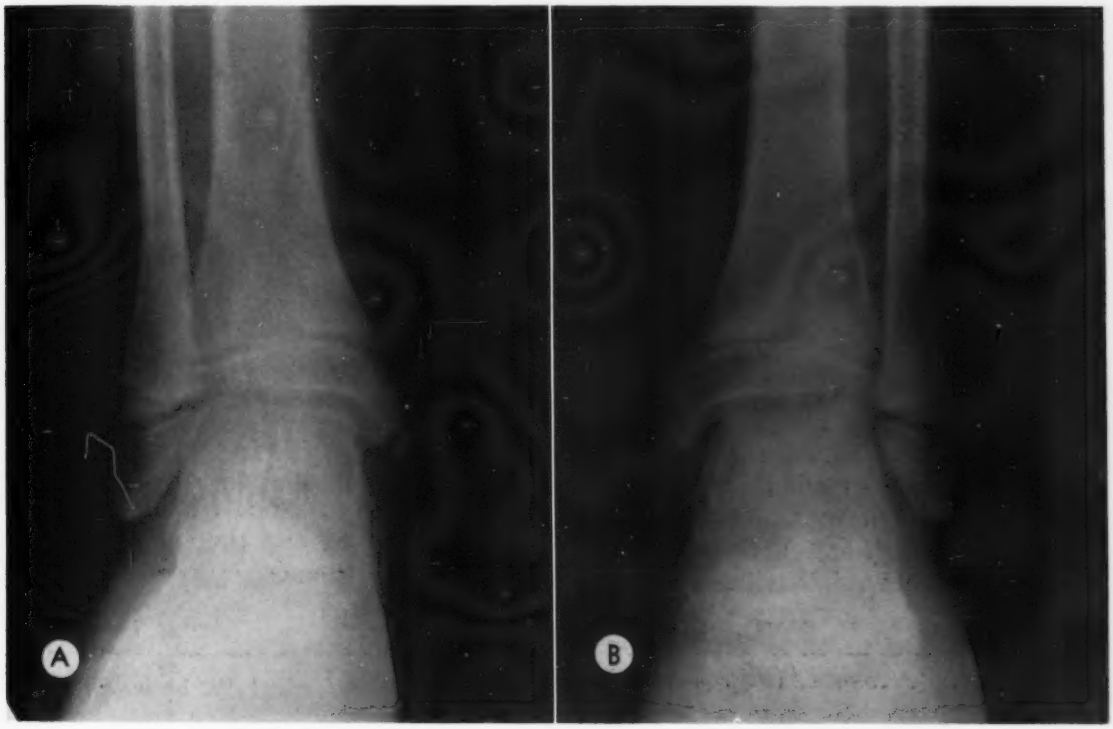

Fig. 7. (*A* and *B*) Female, aged seven and one-half years. Roentgenograms show the formation of the tip of the internal malleolus in an early maturer.

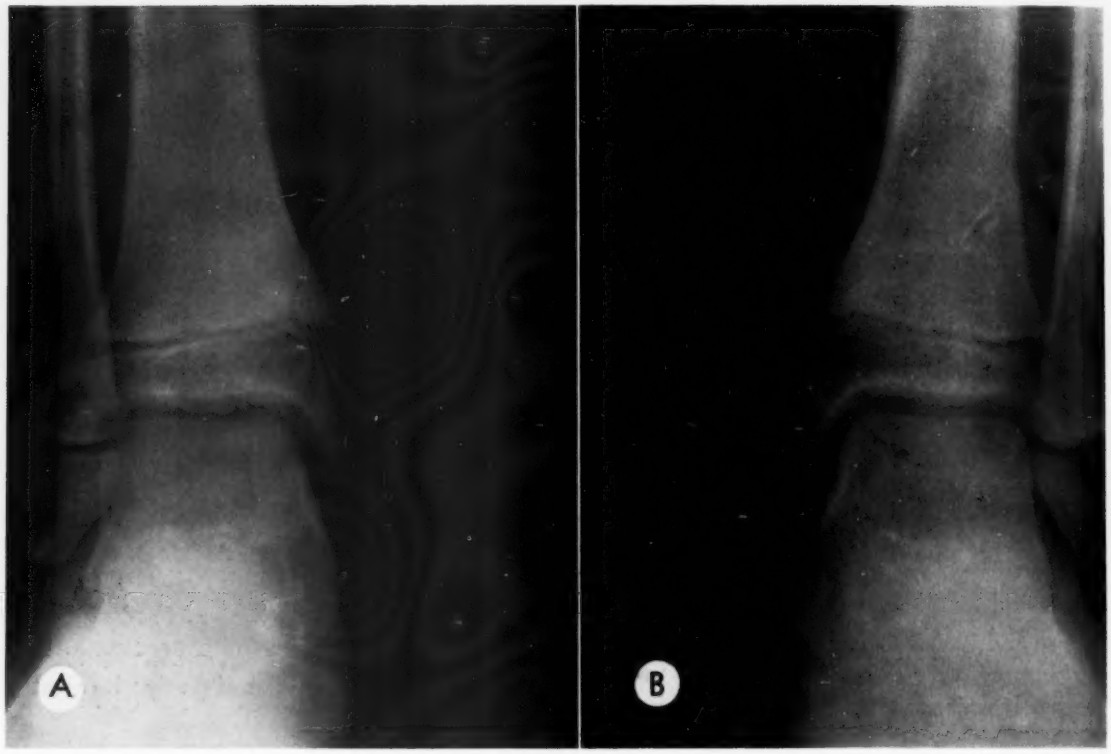

FIG. 8. (*A* and *B*) Female, aged seven and one-half years. Roentgenograms showing that the tip of the malleolus of the right extremity formed ahead of the one of the left extremity.

peared uniformly in all 3 children. Extra ossification centers were regarded as such only when there was a definite radiolucent boundary between the extra center and the main mass of the lower tibial eipiphysis (Fig. 1 and 2). This was the defining boundary which Bircher[1] used in his description of the os subtibiale (Fig. 3). It was found necessary to do this because the rapid downgrowth of calcification, often comma-shaped, could be confused with an extra center. Frequently, there was downgrowing calcification engulfing and surrounding the extra centers which made them look like a conjoined group of spherules (Fig. 4), or multiple centers (Fig. 5). Sometimes the center began as a small millet seed (or it could be larger), then from time to time appeared as two to three discrete small centers (Fig. 6). At times (Fig. 7, *A* and *B*) a separate center of the tibia would appear on the right side before one appeared on the left, or an ossification center on one side might form a tip of the tibia without an extra center (Fig. 8, *A* and *B* and 9, *A* and *B*).

There does not seem to be a uniform pattern in the formation of separate centers of ossification; however, they do tend to be bilateral in females.

CONCLUSIONS

Extra centers of ossification at the tip of the internal malleolus are found more frequently in females than in males. They have been noted in 47 per cent of females. This appears to be a hereditary trait.[9] Pryor[10] observed also that in females the skeletal ossification occurs at an earlier age.

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I am indebted to Christabel Rohmann for statistical help and to Lois Conklin for her patience in typing this article.

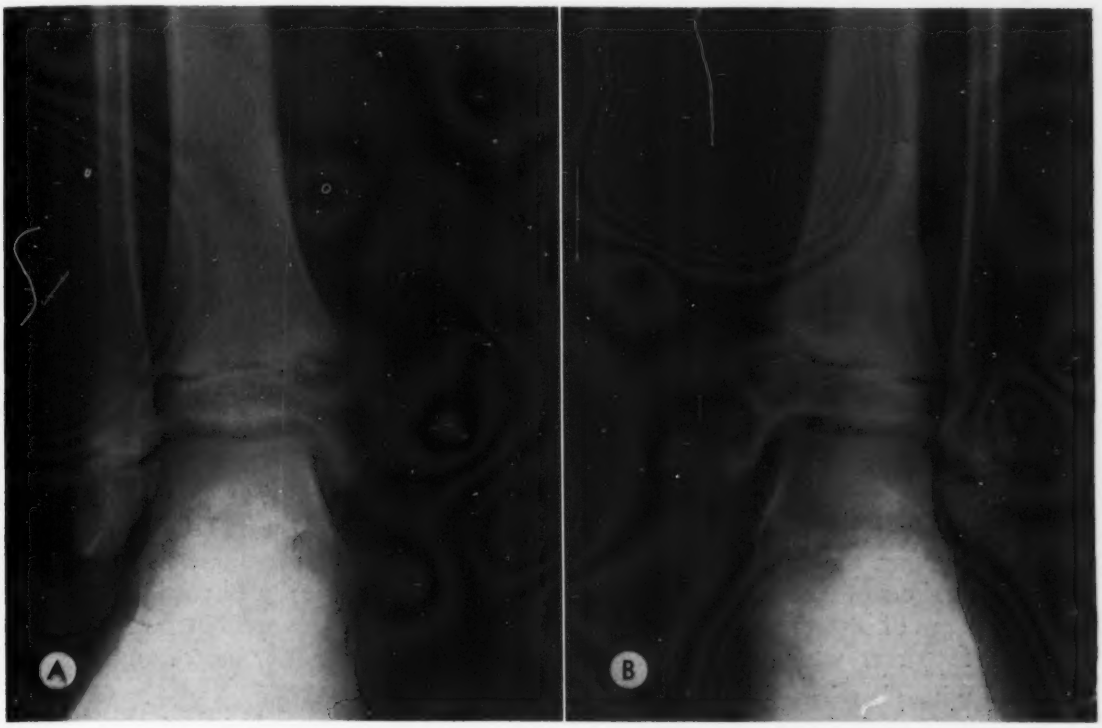

Fig. 9. (*A* and *B*) Female, aged eight and one-half years. Roentgenograms show that the tips of the malleolus are formed in both extremities; however, the right is more advanced than the left. Variations in radiolucency can be seen on the left extremity.

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UNUSUAL BONE TUMORS AFTER ROENTGEN THERAPY OF CHILDREN*

TWO CASE REPORTS

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POSTIRRADIATION tumors of bone, both malignant and benign, have occurred infrequently following roentgen therapy which included exposure of parts of the normal skeleton (Tables 1A and 1B).[26] The appearance of two unusual tumors of bone in a selected series of 247 children who received roentgen-ray therapy at The Children's Hospital Medical Center of Boston has important implications regarding the late effects of radiation in children. The tumors are of interest because of their histologic features, which are distinctly different from any postirradiation tumors of bone previously recorded and which present some difficulty in classification. In the series, the 2 cases represent the only instances of neoplasms, excluding exostoses, which occurred in normal bone after roentgen therapy. In the literature, the most frequent malignancies induced in bone by irradiation have been osteogenic sarcomas. Rarely, chondrosarcomas, giant cell sarcomas, and unclassified sarcomas have appeared. The reported benign postirradiation neoplasma have been osteochondromas.

MATERIAL

The series of children under discussion was selected from the total of 8,321 who were referred to the Radiotherapy Section of The Children's Hospital Medical Center of Boston from January, 1938 to December, 1957. With rare exceptions, all were under thirteen years of age.

They could be classified in two main groups. In the first, 7,423 had benign processes, *e.g.*, hemangiomas, nasopharyngeal lymphoid hyperplasia, keloids, etc. Not all these children were treated. When roentgen irradiation was given, the estimated doses to bone were very rarely more than 1,000 r and, in the majority of patients, less than 500 r. These children, therefore, received lower doses than might be expected to cause bone tumors. They have been followed for many years, either in hospital clinics or by referring physicians. To the best of our knowledge, no instance of postirradiation bone tumor has occurred. Consequently, this group is excluded from further consideration here.

The second group includes 898 children who received more intensive and protracted courses of treatment, the majority for malignant processes, a smaller number for Hand-Schüller-Christian disease or its variants, and a few for aneurysmal bone cysts, nasopharyngeal fibromas, etc. Follow-up data on all but 35 of these children are available. Two hundred and forty-seven have survived for two years or longer after roentgen therapy (Table II). All had treatment administered to portals that included at least one normal bone. The bones most commonly irradiated were the vertebrae, the ribs, and the skull. Of the 247 patients, 207 (84 per cent) had doses of 1,000 r or more delivered to bone.

REPORT OF CASES

CASE 1. R.O. was first seen on January 14, 1943 when he was ten months of age. His chief complaint was a mass in the left flank. He was admitted to the hospital where a clinical diag-

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TABLE 1A

REPORTED BONE TUMORS ARISING IN *NORMAL BONE* AFTER ROENTGEN THERAPY DURING CHILDHOOD

No.	Age When Treated (yr.)	Sex	Latent Period (yr.)	Primary Disease	Bone Affected	Estimated Dose Delivered to Bone	Tumor Type	Reported by
1	11	M	3	Tuberculous knee	Femur	Not stated	Osteogenic sarcoma	Beck[1]
2	6	M	6	Tuberculous knee	Femur	Not stated	Giant cell sarcoma	Marsch[23]
3	9	M	8	Tuberculous knee	Femur	Not stated	Chondrosarcoma?	Marsch[23]
4	7	M	8	Tuberculous knee	Femur and tibia	Not stated	Giant cell sarcoma	Jaruslawsky[14]
5	8	F	3	Tuberculous knee	Femur	Not stated	Osteogenic sarcoma	Küttner[16]
6	5	F	7	Tuberculous knee	Femur	Not stated	Osteosarcoma	Denks[6]
7	11	M	8	Tuberculous knee	Tibia	Not stated	Osteogenic sarcoma	Denks[6]
8	11	F	5	Tuberculous knee	Femur	Not stated	Chondrosarcoma?	Gruca[10]
9	4	M	12	Soft tissue sarcoma	Femur	7,700 r	Osteosarcoma	Cade[2]
10	1	F	10	Retinoblastoma	Frontal	?	Osteosarcoma	Skolnik *et al.*[27]
11	2	F	8	Retinoblastoma	Ethmoid or maxilla	>12,000 r	Osteosarcoma	Tebbet and Vickery[28]
12	12½	M	3	Poliomyelitis	Femur	6,800 r	Osteosarcoma	DeYoung[7]
13	?	?	20	Wilms's tumor	Rib	?	Osteosarcoma	Lichtenstein[19]
14	1 mo.	F	13½	Cystic hygroma	Clavicle	?	Osteosarcoma	Cruz *et al*[5]
15	2	F	6	Retinoblastoma	Ethmoid	25,000 r	Osteosarcoma	Cahan *et al.*[3]

TABLE 1B

REPORTED BONE TUMORS ARISING IN *ABNORMAL BONE* AFTER ROENTGEN THERAPY DURING CHILDHOOD

No.	Age When Treated (yr.)	Sex	Latent Period (yr.)	Primary Disease	Bone Affected	Estimated Dose Delivered to Bone	Tumor Type	Reported by
1	9	M	7	Granuloma	Maxilla	175 r + 1,200 mg./hr. Ra	Osteogenic sarcoma	Sabanas *et al.*[26]
2	10	M	13	Bone cyst	Humerus	6,000–9,000 r	Osteogenic sarcoma	Cahan *et al.*[3]
3	7	M	17	Bone cyst	Femur	1,550 r	Chondrosarcoma	Cahan *et al.*[3]
4	12	M	9	Bone cyst	Humerus	5,580 r	Osteogenic sarcoma	Cahan *et al.*[3]
5	13	F	13	"Cloudiness of antrum"	Maxilla	3,600 r	Osteogenic sarcoma	Cahan *et al.*[3]
6	1	F	7	Bone cyst	Tibia	?	Chondrosarcoma	Francisco *et al.*[8]
7	5	M	7	Bone cyst	Humerus	?	Osteogenic sarcoma	Cruz *et al.*[5]
8	12	M	5	Bone cyst	Humerus	?	Fibrosarcoma	Jaffe[12]
9	9	F	7	Aneurysmal bone cyst	Femur	2,600 r	Fibrosarcoma	Lichtenstein[20]

TABLE II

SELECTED SERIES OF CHILDREN TREATED AT THE CHILDREN'S HOSPITAL MEDICAL CENTER (JANUARY, 1938 THROUGH DECEMBER, 1957) WHO SURVIVED TWO YEARS OR LONGER

Diagnosis	100–499 r	500–900 r	1,000–1,900 r	2,000–2,900 r	3,000–3,900 r	4,000–4,900 r	5,000–5,900 r	6,000–6,900 r	7,000+ r	Total No. of Cases
Central Nervous System Tumors	1	2	8	19	16	9	3	3	2	63
Wilms's Tumor	0	0	9	21	18	7	1	1	0	57
Neuroblastoma	1	1	11	17	6	1	1	0	0	38
Hand-Schüller-Christian Disease	3	22	6	0	0	0	0	0	0	31
Lymphoma	0	2	11	5	2	0	0	1	0	21
Others	4	4	11	8	6	2	0	1	1	37
Total	9	31	56	70	48	19	5	6	3	247

nosis of Wilms's tumor (embryoma) of the left kidney was made. The family history was noncontributory, as was the child's gestational, neonatal, and developmental history.

Physical examination elicited normal findings except for a large, firm, smooth mass in the left flank. The tumor extended from the costal margin to the iliac crest and from the lateral abdominal wall to the midline.

Routine laboratory studies were within normal limits, except for nonprotein nitrogen of 45.2 mg./100 cc. Roentgenograms of the chest and long bones were negative. An intravenous pyelogram showed a large, poorly circumscribed soft tissue mass on the left, without abnormality of the right kidney and ureter.

On January 15, 1943 a laparotomy was performed. The tumor had infiltrated the posterior peritoneal wall, adjacent lymph nodes, and the renal vein. It was irregularly lobulated and arose from the lower pole of the kidney. It could not be completely removed and a left nephrectomy was done. Histologically, the tumor was composed of large sheets and islands of neoplastic cells. There was invasion of surrounding tissues, including the vessels. The pathologic diagnosis was embryoma.

Following the nephrectomy, roentgen therapy was administered with the following technical factors: 200 kvp.; 0.5 mm. Cu and 1 mm. Al added filtration (half value layer of 1.05 mm. Cu); 10 ma.; 50 cm. target skin distance. The free air dose rate at 50 cm. was 28 r per minute. (The doses which follow are all expressed as measured in air.) Daily, except Sundays, 200 r was administered to alternating anterior and posterior portals. The fields, which measured 9.5×13 cm. extended from the right paravertebral plane to the left flank and from the level of D6 to S2. Fifteen treatments in nineteen days (January 16 to February 3, 1943) were given, with total doses of 1,400 r and 1,600 r to the anterior and posterior portals, respectively.

The child did well and was readmitted on June 6, 1944, at which time no recurrence of the tumor was evident. Roentgen therapy was again given, the technical factors being the same as those listed above. Opposing anterior and posterior ports were used, this time measuring 9×12 cm. After an initial treatment of 200 r on June 8, 1944, the daily dose was changed to 300 r, and seven additional treatments in eight days were delivered. The course terminated on June 16, 1944. Thus, a total dose of 1,100 r was given to the anterior portal and 1,200 r to the posterior portal.

Calculations based on the above data were made for the total doses delivered to the left posterior rib cage (1 cm. below the skin) and to the tumor bed at the midplane. Standard depth dose tables[9] were employed and no corrections were made for the lack of homogeneity of the irradiated tissues, uneven distribution of dose across the field, etc. The figures which follow are approximations and are not meant to be precise assessments of the doses delivered. Thus, 2,566 r was received by the posterior portions of the ribs in the first course of roentgen therapy, while the tumor dose was 1,950 r as calculated at the midplane. The corresponding dosages during the second course were, 1,697 r and 1,357 r, totalling 4,263 r and 3,307 r to ribs and tumor, respectively. Using an appropriate conversion factor, the estimated rib dose in rads was 7,503.[24]

Following this therapy the boy was seen at intervals and continued to do well. When he was fifteen years old, thirteen years after the completion or roentgen therapy, he first felt a lump in his chest which was slightly tender and painful. Two weeks thereafter he was readmitted to the hospital. At this time, physical examination revealed a well-healed left rectus incision and no other abnormal findings except for a firm tender mass 3 cm. in diameter, associated with the eleventh left rib. Routine laboratory examinations were normal except for occasional hyaline casts in the urine.

Roentgen examination (Fig. 1) showed an irregularity of the bodies of the lumbar vertebrae, without erosion or destruction. The left ilium was small and underdeveloped. A mild scoliosis in the thoracolumbar area was noted. The left eleventh rib showed an irregular architecture and expanded contour, with mottled density and punctate calcific deposits within a surrounding soft tissue mass.

Operation on September 4, 1957 disclosed a firm mass, 4×3×5 cm., involving the eleventh rib. The cut surface showed several segments of paper-thin bony cortex which was entirely absent over the medial aspect. The tumor, a solid, nodular, white, and translucent mass, extended through the pleura, which was not infiltrated. An *en bloc* excision was performed, with the removal of the tenth, eleventh, and twelfth ribs by disarticulation from the vertebrae. The associated soft tissues, including intercostal

muscles, blood vessels and nerves, were also excised.

Microscopically (Fig. 2; and 3, *A–C*), the tumor was found to have broken through a thin bony cortex at a number of places and to have extended into the adjacent fibrous tissue but not into the muscle. Nodules of abnormal cartilage, separated by thin fibrous septa, comprised most of the tumor. The centers of the nodules were often composed of mature cartilage with fewer cells and more matrix than in the periphery. Myxoid tissue was present in abundance. The cartilage cells were variable in shape and size and many had atypical nuclei and occupied large lacunae, some of which contained two and three cells. No gaint cells, areas of calcification, or bone formation were noted. In the periphery

Fig. 1. Case 1. A fifteen year old boy with a bone tumor developing thirteen years after roentgen therapy of the left hemiabdomen. The left eleventh rib, normal at the time of irradiation, now shows expansion and irregularity of outline. There is disruption of the normal bony architecture. Mottled calcification is present within an associated soft tissue mass. Postirradiation abnormalities in the contour and size of the left ilium and of the dorsal and lumbar vertebrae are visible.

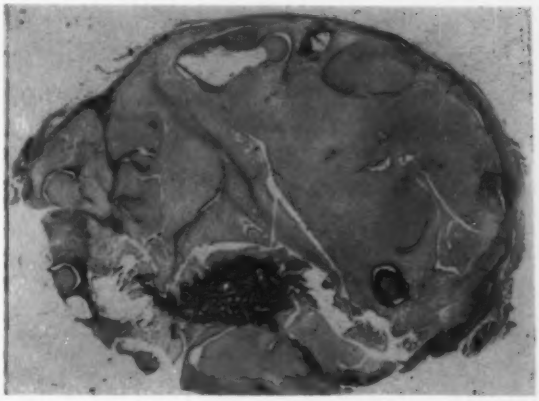

Fig. 2. Case 1. Low power magnification of a cross section of the tumor. The bony portion of the rib is surrounded by tumor the lobulation of which is evident. The smaller, darker-stained lobules contain calcified cartilage. Small plaques of bone are seen in the left upper and right lower portion. The pleura is at the inferior edge of the mass.

of some nodules, rows of cells were present which resembled fibroblasts separated by cords of atypical nonfibrillar matrix.

Postoperatively the boy did well and two years later showed no evidence of tumor. However, the scoliosis (apex at D10) showed a marked increase and at that time measured 15° in recumbency and 25° in the upright position. No symptoms were present.

Case II.* B.H., a Negro girl, first complained of abdominal swelling and vomiting in April, 1954, when she was three years old. At another hospital, physical examination revealed an abdominal mass which was diagnosed as Wilms's tumor. It was found to infiltrate the liver and, during its removal, it was excised "flush with the liver" but abdominal spillage of tumor cells occurred. Her postoperative course was stormy and was complicated by hemorrhage, shock, suture of a partially divided common iliac artery, and adrenal insufficiency requiring prolonged ACTH and cortisone therapy.

Postoperatively, roentgen therapy was given to the right upper abdomen to anterior, lateral, and posterior portals, each measuring 10×15 cm. Air doses of 1,300 r, 1,200 r, and 1,000 r, respectively, were given to these three portals from April 8 to 27, 1954. The technical factors

* Details regarding the early roentgen treatment given this patient are reported through the kind cooperation of Dr. B. B. Alicandri, Mercy Hospital, Springfield, Massachusetts.

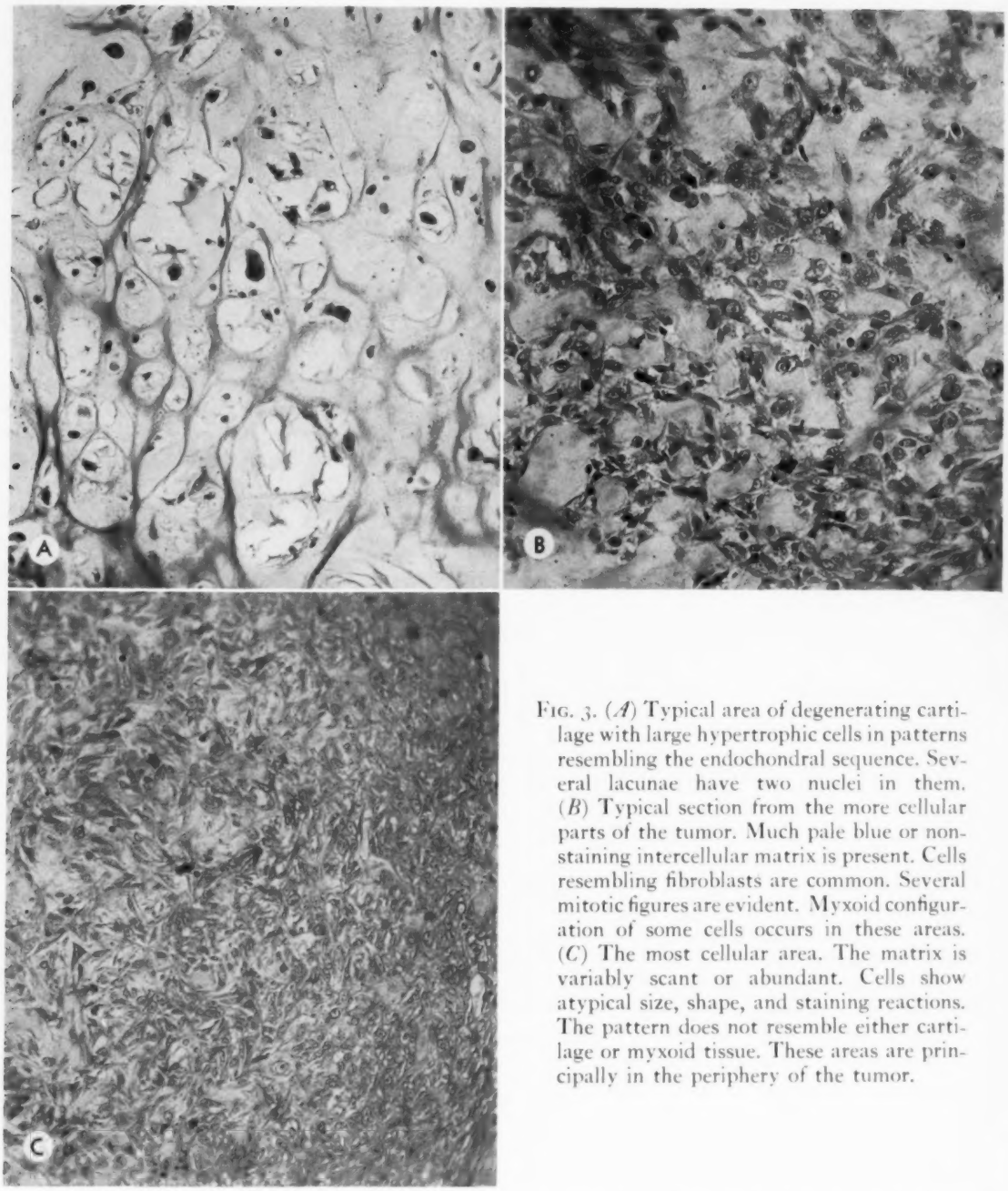

FIG. 3. (*A*) Typical area of degenerating cartilage with large hypertrophic cells in patterns resembling the endochondral sequence. Several lacunae have two nuclei in them. (*B*) Typical section from the more cellular parts of the tumor. Much pale blue or nonstaining intercellular matrix is present. Cells resembling fibroblasts are common. Several mitotic figures are evident. Myxoid configuration of some cells occurs in these areas. (*C*) The most cellular area. The matrix is variably scant or abundant. Cells show atypical size, shape, and staining reactions. The pattern does not resemble either cartilage or myxoid tissue. These areas are principally in the periphery of the tumor.

employed yielded a half value layer of 1 mm. of Cu; the target skin distance was 50 cm. From June 9 to 19, 1954, an additional 1,200 r in air was given to a posterior portal directed to the right upper renal fossa through a 10×10 cm. field. At the same time, treatment was directed to a left hilar nodule, employing 10×10 cm. opposing thoracic portals. An air dose of 660 r was given to the anterior chest and 1,200 r to the posterior. The depth dose was calculated at the level of the left rib cage posteriorly (1 cm. below the skin) and in the midplane in the same manner as in Case 1. The total estimated dose to the midplane was 1,246 r and to the posterior ribs, 1,800 r (3,168 rads).

After this therapy the liver began to enlarge and on August 11, 1954 the patient was first referred to this hospital. At that time physical ex-

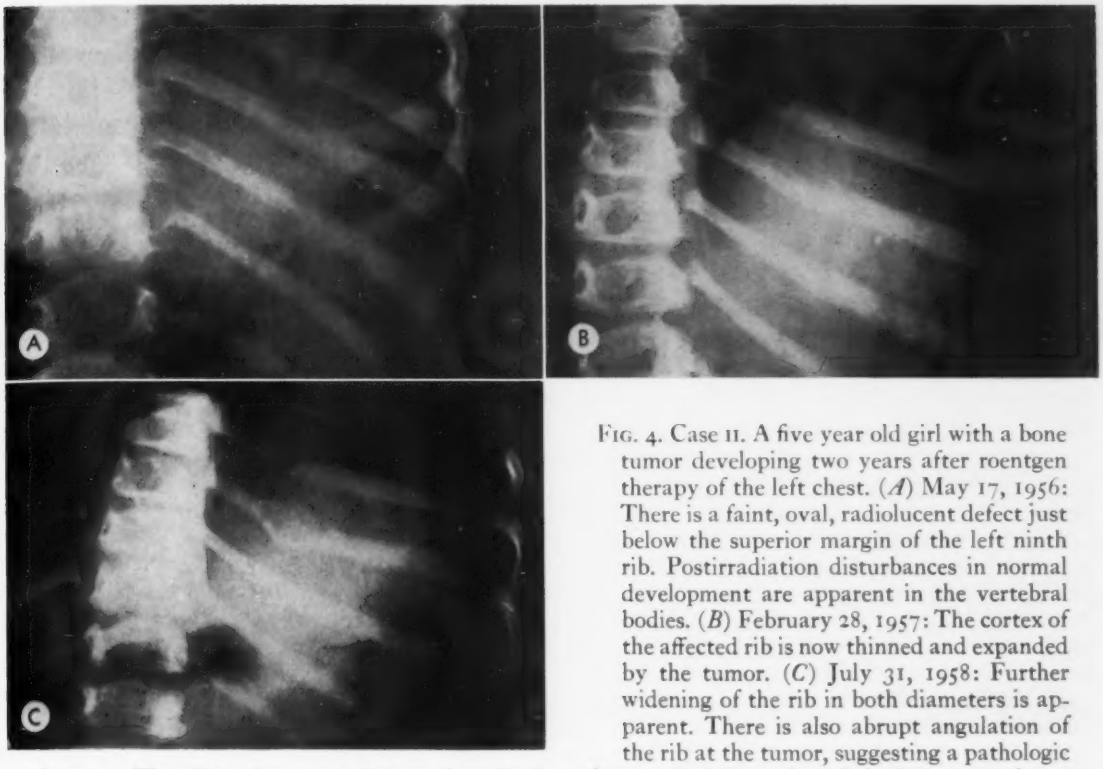

Fig. 4. Case 11. A five year old girl with a bone tumor developing two years after roentgen therapy of the left chest. (*A*) May 17, 1956: There is a faint, oval, radiolucent defect just below the superior margin of the left ninth rib. Postirradiation disturbances in normal development are apparent in the vertebral bodies. (*B*) February 28, 1957: The cortex of the affected rib is now thinned and expanded by the tumor. (*C*) July 31, 1958: Further widening of the rib in both diameters is apparent. There is also abrupt angulation of the rib at the tumor, suggesting a pathologic fracture. The thinned cortex is intact along both surfaces and the margins of the lesion are sharp, without infiltration of the adjoining rib shaft. No soft tissue mass is visible.

amination showed a poorly developed girl whose principal physical findings indicated a fading radiodermatitis of the abdominal wall and a slight enlargement of the liver. The laboratory findings were within normal limits and the roentgenographic survey of the chest and skeleton showed only an increase in lung markings which was interpreted as radiation fibrosis.

Treatment with a number of antitumor chemotherapeutic agents was then begun and continued intermittently until the present. The child did well until November, 1954, at which time sudden flaccid paralysis of the right lower extremity without sensory loss was noted. She was again hospitalized and a presumptive diagnosis of anterior poliomyelitis was made after myelograms and other pertinent tests did not reveal any other explanation for the paralysis. The neurologic findings have persisted to the present; otherwise, the patient has been asymptomatic, albeit underweight and slow in developing.

In September, 1958, a lesion of the ninth left rib which expanded the cortex was discovered on routine roentgenography. Retrospectively, the lesion could be seen as early as May 17, 1956, at which time it was merely a juxtacortical radiolucency, 2 cm. in length, within the rib shaft and evident posteriorly (Fig. 4*A*). Serial roentgenograms showed gradual growth of the lesion, which had begun to expand the cortex (Fig. 4, *B* and *C*). By September, 1958 it measured 2.0×1.3 cm. and had widened the rib in an irregular fashion. No palpable mass was present.

On September 19, 1958 a segment of the ninth rib was removed. The resection included periosteum and normal bone on both sides. At operation, no invasion of soft tissues by the tumor was noted. A postoperative roentgenogram taken on September 25, 1959 is shown in Figure 5.

Gross examination of the specimen removed at operation revealed a recent fracture through the thin cortex. The cancellous bone of the marrow was replaced by gray, firm, fibrous tissue which, on section (Fig. 6, *A*, *B* and *C*), showed densely packed cells with variable

FIG. 5. Case II. September 25, 1959: Postoperative roentgenogram shows that a portion of the left ninth rib posteriorly is absent and there is a small osteochondroma of the right ilium. Postirradiation scoliosis and underdevelopment of the right innominate bone are also present.

amounts of cellular matrix between them. The patterns of the matrix ranged from fairly mature trabecular cancellous bone to primitive fibrillar collections between masses of cells. Foci of giant cells were present. No cartilage, fibrosis, inflammation, or degeneration was present. None of the cells showed atypical nuclear staining, and mitotic figures were infrequent.

DISCUSSION

Only circumstantial evidence supports the contention that radiation has caused neoplasms to develop in cases such as those reported here. Points in favor of this cause-and-effect relationship in the present cases are: (1) the involved ribs showed no abnormality before irradiation. There is no roentgen or histologic evidence to suggest that the tumors arose in pre-existing abnormalities of the bone substance. (2) The dose of radiation was sufficient in both patients to cause growth disturbances in areas immediately adjacent to the involved ribs. (3) The incidence of primary tumor in ribs is infrequent and only a few cases have been reported. It is highly improbable, therefore, that these 2 tumors were primary, spontaneous lesions not associated with irradiation but arising coincidentally in the small group of patients who comprised the selected series. (4) Evidence for the carcinogenic action of irradiation on bone is well documented experimentally and clinically with respect to radium and mesothorium, and experimentally with respect to other bone-seeking radioisotopes. There are only a few reports of the possible carcinogenic potency of local external roentgen irradiation in animals.[17,18,21,22] Perhaps the long latent periods and paucity of postirradiation bone tumors in patients have discouraged experimental studies on this subject. The frequency with which these neoplasms develop in bone is not known with certainty. They must be rare because only 86 cases have been reported. It is noteworthy that 24 of these were in children thirteen years old or younger at the time of irradiation. This frequency in children of over 25 per cent of the reported cases is markedly disproportionate, since children make up only a small fraction of the patients seen in a general radiotherapy center. In 15 of the 24 children listed in Table 1A, neoplasms developed in normal bones included in the field of roentgen therapy. Only 1 of these children received treatment for Wilms' tumor. He developed an osteogenic sarcoma in a rib, the same bone affected in our 2 patients. No other rib tumors developed in the children listed in Tables 1A and 1B.

The relationship between total roentgen dose, dose rate, and latent period, and the development of bone tumors (malignant and benign) is not clearly defined. Jones[15] has published a comprehensive report on the problem of dosage in postirradiation sarcoma. On the basis of his own experience and the experience of others, he supports

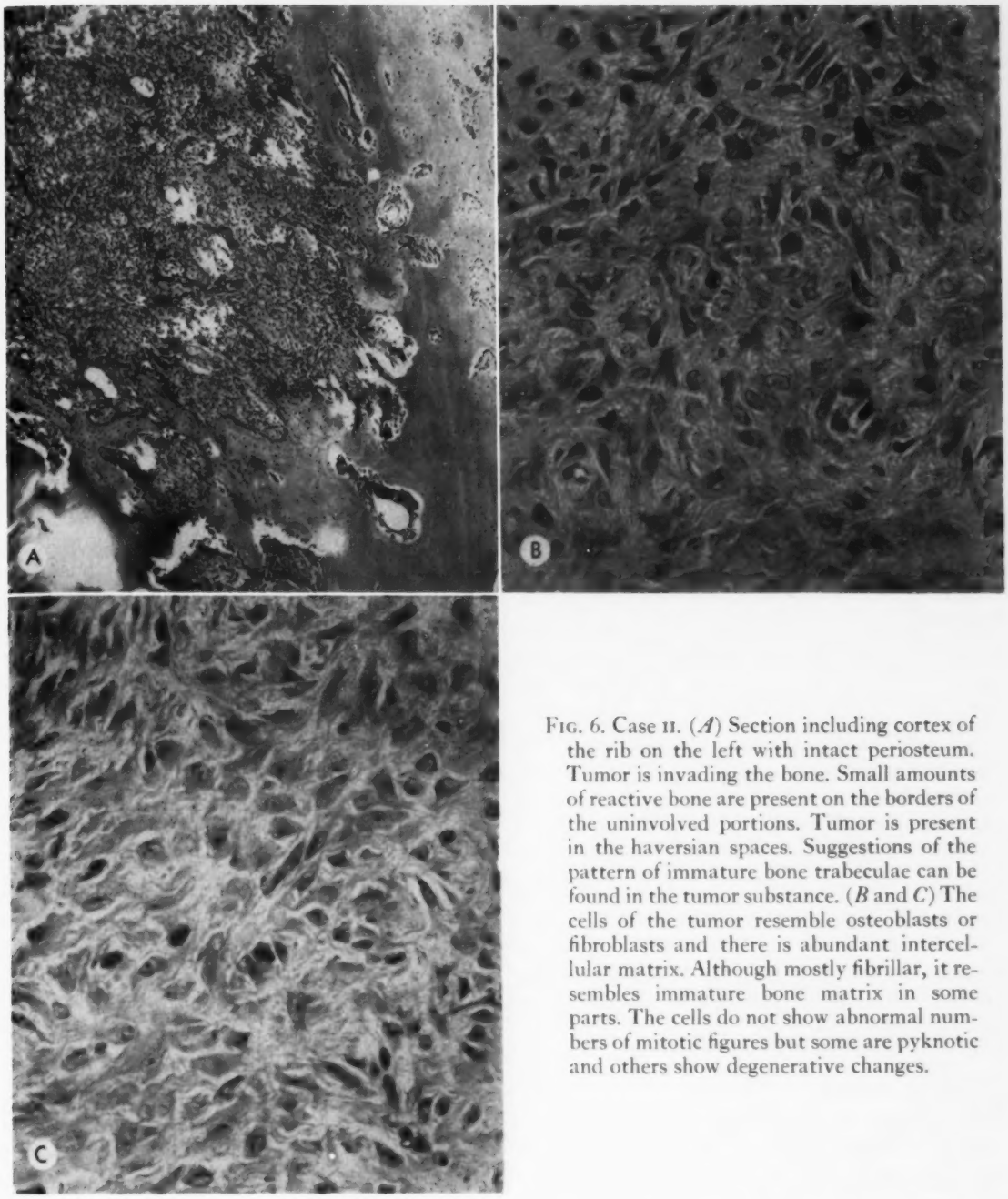

Fig. 6. Case 11. (*A*) Section including cortex of the rib on the left with intact periosteum. Tumor is invading the bone. Small amounts of reactive bone are present on the borders of the uninvolved portions. Tumor is present in the haversian spaces. Suggestions of the pattern of immature bone trabeculae can be found in the tumor substance. (*B* and *C*) The cells of the tumor resemble osteoblasts or fibroblasts and there is abundant intercellular matrix. Although mostly fibrillar, it resembles immature bone matrix in some parts. The cells do not show abnormal numbers of mitotic figures but some are pyknotic and others show degenerative changes.

the contention advanced by Cahan *et al.*[3] that a threshold dose of about 3,000 r is necessary for the production of malignant tumors. Two extensive reviews[5,26] and several additional case reports have since appeared. In some patients in whom the dose could be estimated accurately, secondary malignant bone tumors developed after small doses—for example, 1,000 r. More often, however, the level of 3,000 r was exceeded.

The latent period in the 38 cases reviewed by Jones[15] ranged from 3 to 22 years from the end of irradiation, with a mean interval of 8.6 years. The latent period in our second case (two years) is the

shortest hitherto recorded in children (Tables 1A and 1B), while the latent period in our first patient is well beyond the average reported.

Several reviews on the histology of post-irradiation sarcoma of bone have been published. Sabanas *et al.*,[26] in 1956, summarized the 53 cases recorded in their bibliography and added 17. Most of them had radiation therapy for various types of lesions of bone, and the sarcomas, therefore, arose in pathologic tissue which had been irradiated. Only 3 of their own cases and 10 among those they had reviewed occurred in normal bones which happened to be in the path of radiation administered for adjacent lesions. Three patients developed osteogenic sarcomas, which appeared thirteen, twenty-one, and thirty years after radiation therapy. In the 10 cases which they reviewed, osteogenic sarcomas also predominated, the exceptions being 1 case reported by Copeland[4] (fibrosarcoma superimposed on periosteal osteoma) and 3 reported by Hatcher[11] (chondrosarcoma). Since the study of Sabanas *et al.* was published, 6 additional reports have added 16 cases to the total of bone sarcomas as sequelae to irradiation, administered mostly to adults. Ten of these tumors occurred in previously normal bone tissue. Of these, the 4 cases reported by Cruz *et al.*[5] in 1957 were osteogenic sarcomas, as were 5 of the other cases reported. The tenth was a fibrosarcoma reported by Cade.[2]

From the histologic data in the articles reviewed, only 2, or possibly 3, instances of chondrosarcoma have been recorded subsequent to irradiation of previously normal bone. Cartilage is present in many post-irradiation osteogenic sarcomas. The same is true of the experimental postirradiation sarcomas after administration of radioisotopes. However, cartilage rarely has been the predominant tissue in the clinical cases, as it was in our patient, R. O. (Case 1). His tumor was distinctly different from the others in the literature for which histologic data are presented, including the chondrosarcomas reported. Hatcher's 3 patients showed areas of reactive bone formation and fibrous elements of neoplastic type, in addition to malignant cartilaginous tissue. The tumor in our Case 1 did not contain any elements other than cartilage and myxoid tissue. Although lobulated, the cartilage and myxoid structure was extensive and confluent, a finding not seen in postirradiation osteogenic sarcomas. In those cases, cartilage when present usually was found in small nodules interspersed in the main tissue mass.

There was a wide diversity of opinion on the diagnosis of the tumor in our patient, R. O. The authors and some consultants believed it represented a chondrosarcoma. Others have thought that the tumor was nonmalignant, *i.e.*, either a chondromyxoid fibroma or a chondroma. A diagnosis of chondromyxoid fibroma is usually based on the presence of numerous areas of myxoid tissue in which the cells show some bizarre features. These were occasionally seen in the lesion of R. O. Though the cortex was breached, there was no unequivocal extension into the surrounding muscle, so we cannot exclude the possibility that fibrous tissue still encompassed the tumor. However, the clinical history of rapid enlargement of a painful tender mass argues against the diagnosis of chondromyxoid fibroma. Jaffe's 2 patients,[12,13] each with a chondromyxoid fibroma in a rib, were asymptomatic and the diagnosis was incidental to roentgen examination of the chest. The roentgen evidence of punctate calcification present in our patient does not support the diagnosis, even though it might be suggested by the radiolucency and expansion. As Jaffe points out, the distinctions between chondromyxoid fibroma, with or without malignant transformation, and chondrosarcoma of primary type are often difficult to draw. R. O.'s lesion represents one in which histologic diagnosis is difficult, and in which the future course of the patient may illuminate the pathology further.

In our Case 11, there was also some disagreement concerning the exact histologic diagnosis. The authors and most of the

consultants who saw the lesion thought it represented an osteoblastoma. Several others felt that the lesion was not a tumor, but rather an abnormal reparative reaction subsequent to a fracture. In support of this latter possibility is the known occurrence of fractures in irradiated bone. This has been reported not only in the femoral neck after roentgen treatment of carcinoma of the cervix, but also in ribs following therapy for breast carcinoma. The time interval between cessation of treatment and the development of the lesion also corresponds to that described for post-irradiation fractures (usually one to five years), rather than that described for post-irradiation tumors (often more than eight years). However, most of the reported fractures were not examined histologically. Roentgenologically, they did not resemble the lesion under discussion, nor were they preceded by the appearance of an expanding radiolucent focus in the rib. It is probable that the fracture seen in the patient under discussion was secondary to the replacement of bone by nonosseous tissue, probably neoplastic.

Irradiation of growing bones can lead to disturbances in normal skeletal development. Some of these complications, *e.g.*, scoliosis and exostosis, have been reported by Neuhauser *et al.*[25] and are exemplified by our patients. They both have postirradiation scoliosis and underdevelopment of the ilium. In addition, Case 11 developed an osteochondroma of the right ilium five years after roentgen treatment.

One case reported by Cruz *et al.*[5] is noteworthy in that the patient showed a post-irradiation osteogenic sarcoma in a clavicle and, in addition, an osteochondroma of the adjoining humerus. These complications, together with the relatively high frequency of postirradiation neoplasms, emphasize the need for prolonged and careful surveillance of all children receiving radiation therapy.

SUMMARY

In a selected series of 207 children who received roentgen therapy with 1,000 r or more delivered to bone, 2 subsequently developed neoplasms of bone. Both bone tumors occurred in normal ribs included in the field of treatment. The tumors were atypical; one resembled a chondrosarcoma, the other an osteoblastoma. The latent periods were thirteen and two years, respectively. Both children had postirradiation scoliosis and hypoplasia of the ilium. One also developed an osteochondroma of the ilium.

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Vol. 86, No. 3

CONGENITAL BIFID STERNUM WITH PARTIAL ECTOPIA CORDIS*

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PARTIAL ectopia cordis with congenital bifid sternum is, according to the current literature, a difficult problem for surgical repair and reconstruction. Sabiston,[8] in 1958, reported his successful repair in a child two years of age. The purpose of this paper is to present the case report of a child operated upon in the fourth year of life, using the method of Sabiston, and to discuss the radiologic findings associated with this defect.

REPORT OF A CASE

W.V.F., a four year old white boy, had been noted to have absence of the sternum in the midline since birth. The mother had reported pulsations beneath the skin and the condition had been undiagnosed until a local physician referred him for thoracic surgical evaluation. The child was the thirteenth of 14 pregnancies and there was no family history of any other known congenital deformities. The past medical history was entirely negative except for short episodes of upper respiratory infections and tonsillitis. The physical findings were normal except for the anomaly of the chest. This showed a prominent V-shaped defect in the area of the sternum. The two medial clavicular heads were separated by 5.5 cm. when the patient was in a normal standing position. The xiphoid process was present and united. The edges of the deformity were composed of two sternal bodies. Coughing produced marked bulging in the area of the defect, showing evidence of bilateral pulmonary herniation into the mediastinum. Pulsation of the heart and great vessels was easily detectable by both inspection and palpation. No cardiac abnormalities were discovered. Examination of the skin over the defect showed a 1.5 cm. circular area suggestive of a scar. The skin in this area seemed to be fibrous in quality. There was no drainage present and no past history of any drainage. This area had been visible since birth according to the mother. Complete blood cell count was normal except for eosinophilia. Blood chemistries were within normal limits. Urinalysis was normal. Serology was nonreactive. Stools for ova and parasites showed a few ova of Trichuris trichiura. Electrocardiogram was normal. Chest roentgenograms (Fig. 1, *A* and *B*) showed a wide separation of the sternal ends of both clavicles and widening of the superior mediastinal shadow in the posteroanterior view. This finding was compatible with a clinical diagnosis of bifid sternum with partial ectopia cordis. In the lateral view (Fig. 2, *A* and *B*) there was absence of the manubrial shadow and loss of convexity of the manubrio-sternal junction with concavity in the suprasternal region. Esophagram was within normal limits.

On August 20, 1959 repair of the partial ectopia cordis and bifid sternum was performed under general endotracheal anesthesia. A midline incision was made, extending from 3 cm. below the thyroid cartilage down to the tip of the joined xiphoid process. Full flaps of skin and subcutaneous tissue were raised and the pericardium was visualized beneath these flaps. Skin flaps, subcutaneous tissue and then the muscle layers were reflected from the ribs. The pericardium was freed from the under surface of the unjoined sternal bodies. The perichondrium was freed anteriorly and posteriorly from the cartilages. A triangular wedge of the connected xiphoid was excised. Two temporary sutures were placed around the sternal bodies, and, when these were tied, they reduced the defect approximately one-half its greatest width. The first four costal cartilages on either side were then freed and exposed subperichondrially. Oblique incisions were made in each of these cartilages and circumferential sutures around the bifid sternal bodies completely approximated the defect due to the relaxation afforded by the oblique division of the four superior costal cartilages. The posterior and anterior portions of sternal periosteum were approximated. Circumferential sutures around the sternal bodies were tightly joined. There was no evidence of entrance into the pleural cavities.

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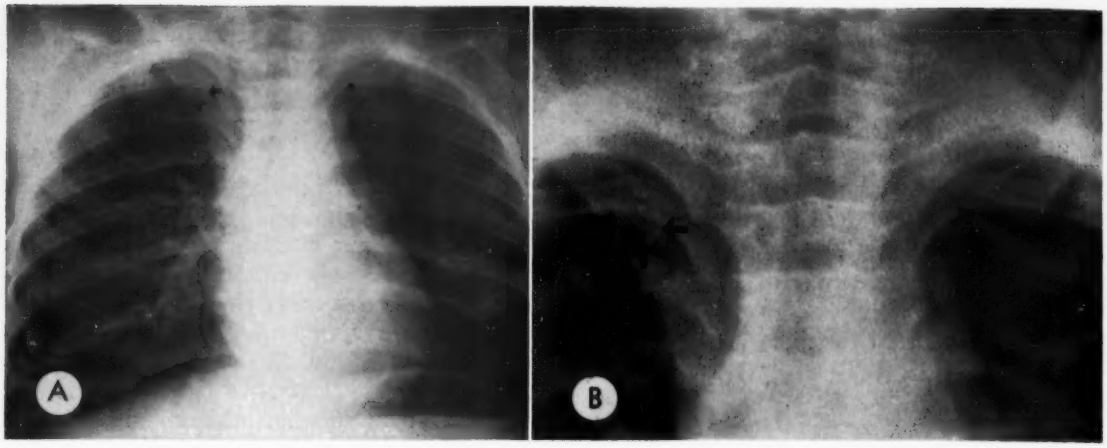

FIG. 1. (*A*) Preoperative roentgenogram of the chest showing wide separation of the sternal ends of the clavicles (arrows) and widening of the superior mediastinal shadow. (*B*) Enlargement of the area of abnormality shown in *A*.

The subcutaneous tissue and skin were approximated.

Motion pictures were made of the entire operative procedure and the immediate postoperative result showed a good functional and cosmetic repair of the preoperative defect. On the evening of operation, a 50 per cent right pneumothorax appeared, and this was completely relieved by aspiration of air from the right pleural cavity. On the first postoperative day, a 30 per cent left pneumothorax was immediately relieved by thoracentesis. Following this, both lung fields remained clear and normal. The boy was given intensive preoperative and postoperative physical therapy and was discharged from the hospital on the seventh postoperative day, completely asymptomatic. One year following operation, physical examination showed an adequate cosmetic and functional recovery. Follow-up roentgenograms (Fig. 3, *A*

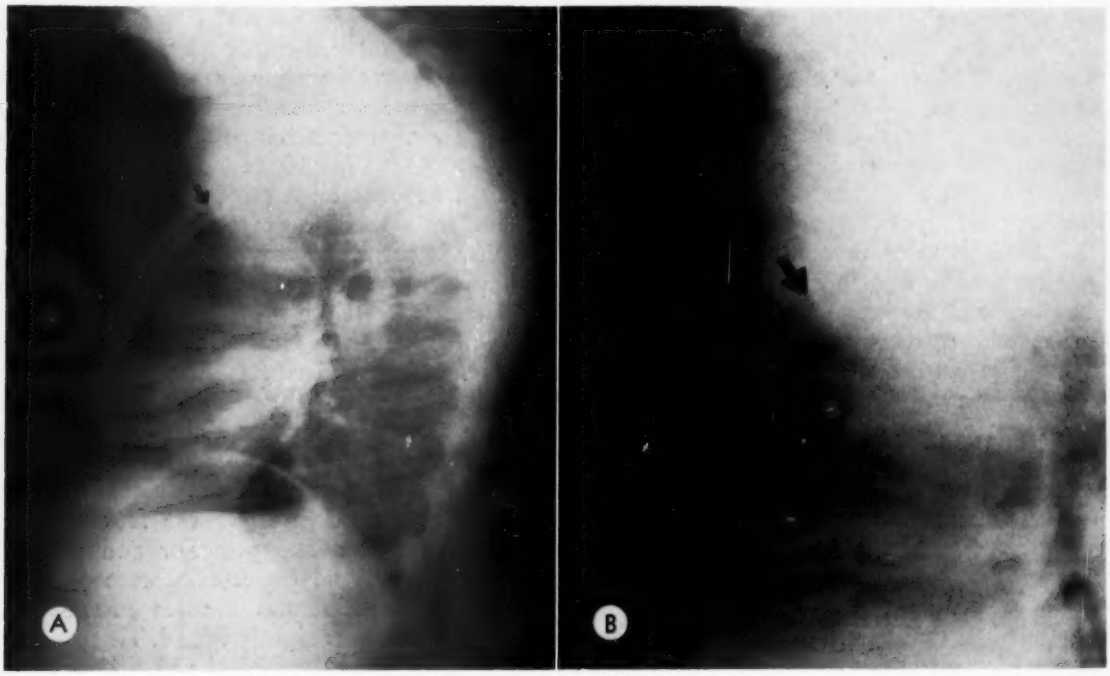

FIG. 2. (*A*) Preoperative left lateral roentgenogram of the chest showing absence of the manubrial shadow and loss of convexity of the manubrio-sternal junction. There is a concavity in the suprasternal region (arrow). (*B*) Enlargement of the area of abnormality shown in *A*.

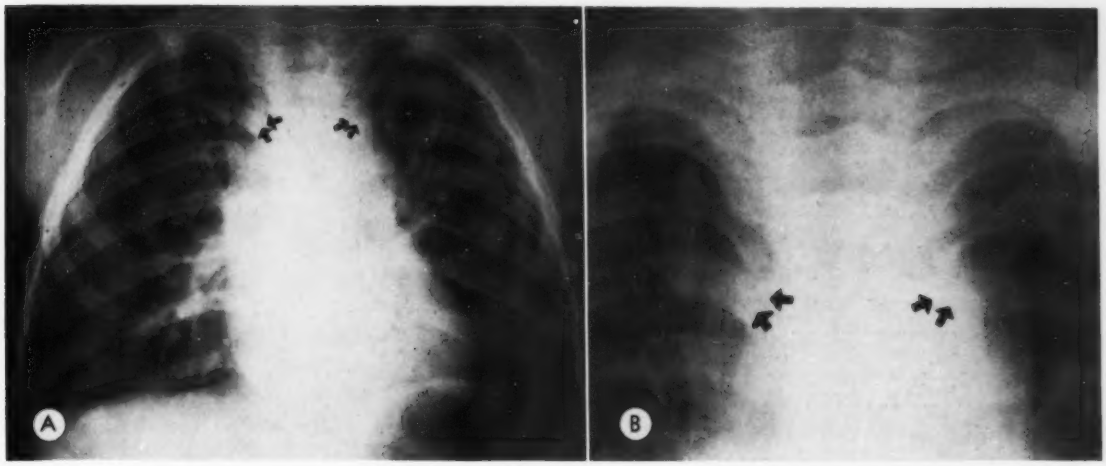

Fig. 3. (*A*) Postoperative posteroanterior roentgenogram of the chest showing approximation of the sternal ends of the clavicles (arrows). (*B*) Enlargement of area shown in *A*.

and *B*, and 4) also showed approximation of the sternal ends of the clavicles.

DISCUSSION

EMBRYOLOGY

In 1885 Madden,[6] reporting a case of congenital fissure of the sternum, was the first to state that the condition was due to a failure of union of the two primitive cartilages from which the osseous sternum is formed. He remarked that this same imperfection was quite frequently seen in hare-lip, often extending to the osseous structures beneath, such as the superior maxillary bone. Spina bifida and exstrophy of the bladder were felt by him to be other examples of the same type of failure of fetal development and nonunion in the midline. Hanson,[3] in discussing the ontogeny and phylogeny of the sternum in animals and man, added much to our understanding of congenital bifid sternum. He demonstrated that the sternum originates separately from the ribs as two longitudinal structures in the anterior thorax. The space between these two sternal bodies is present from the sixth to the ninth week embryo. The bands also fuse laterally with the costal cartilages. It is therefore apparent that in the rare instances of congenital bifid sternum there is a failure of this midline union. A defect results and through it the pericardium may herniate, being covered only by subcutaneous tissue and skin. This is the condition demonstrated in our present case. Gussow,[2] in 1946, first described the surgically unexplained scar-like depression in the midportion of the anterior chest wall. Since then this has been noted by other authors and was definitely present in our case. He remarked that this round scar-like depression suggests an anomaly of the sternum.

Fig. 4. Postoperative left lateral roentgenogram of chest.

ROENTGENOGRAPHIC FINDINGS

Though Gussow[2] stated that the routine roentgenograms of the chest are not of much help in this anomaly, the frontal view of the chest is definitely of diagnostic value.

Wide separation of the sternal ends of the clavicles and widening of the superior mediastinal shadow on the posteroanterior or anteroposterior roentgenograms of the chest are characteristic features of this anomaly (Fig. 1, *A* and *B*). The manubrial shadow is absent. On the lateral roentgenogram there is seen a loss of the usual convexity of the manubrio-sternal junction and the presence of a concavity in the suprasternal region (Fig. 2,*A* and *B*).

SURGICAL CONSIDERATIONS

In 1947, Burton[1] reported his experience in the surgical treatment of congenital bifid sternum with partial ectopia cordis. Both of his cases were treated by a block of cartilage which was removed from the costal margin and placed over the defect. The cosmetic results were only moderately good. In 1949, Maier and Bortone[7] performed a primary surgical closure. A good result was obtained by a direct suture procedure in a six week old infant. In a discussion of Maier and Bortone's paper, Klassen[4] reported a similar case where an attempt at repair was unsuccessful. Longino and Jewett[5] described a successful primary approximation of a bifid sternum in a six day old infant. It is noted that there is general agreement that whenever possible the preferred management should be direct operative closure in early infancy. Sabiston[8] first reported a logical method of repair of congenital bifid sternum with ectopia cordis in older children. The repair which he described was the one used in our case and to our knowledge from a review of the literature the only other case thus treated. Our cosmetic and functional results were considered successful; this was also true in the case reported by Sabiston. The operation was considered simple and effective. The sliding costal cartilage technique offered no difficulty in the correction of the deformity. The present authors agree that with Sabiston's technique there is no necessity for the use of tissue grafts or plastic materials in the repair of this malformation.

SUMMARY

1. A case of successful repair of congenital bifid sternum with partial ectopia cordis in a four year old child has been presented. This is the second successful case known to have been repaired by this method.

2. Bifid sternum with partial ectopia cordis is a very rare anomaly, resulting from failure of union of the two primitive sternal bands.

3. The characteristic roentgen findings are wide separation of the sternal ends of the clavicles and widening of the superior mediastinal shadow in the frontal view of the chest and loss of normal convexity at the manubrio-sternal junction in the lateral view. The manubrial shadow is absent.

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Vol. 86, No. 3

CONGENITAL PARTIAL DEFECT OF THE PERICARDIUM ASSOCIATED WITH HERNIATION OF THE LEFT ATRIAL APPENDAGE*

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CONGENITAL pericardial defect is a very rare anomaly, although Columbus[7] described a case of pericardial defect as early as 1559. The first verified case of congenital absence of the pericardium was reported by Baillie[1] in 1793.

In 1925, Moore and Shumacker[17] reported 64 recorded cases of periocardial defect. More recently Ellis, Leeds, and Himmelstein[9] compiled a total of 99 cases from the medical literature including 2 of their own. The present case report, together with a recent report of 5 such cases by Jones,[12] a single case by Brea *et al.*,[4] and 2 cases by Hering *et al.*,[11] brings the total number to 108.

Partial pericardial defect is less common than complete absence of the pericardium. In some instances when there is a partial defect, there may also be herniation of all or a portion of the heart, and this may lead to the patient's death.

Syncope and sudden death were reported in one case by Boxall[3] and in another by Sunderland and Wright-Smith;[27] in these cases, incarceration and strangulation of the heart were caused by a hernial ring of the pericardium. In our present case, there was a herniation of the left atrial appendage through a partial pericardial defect. Similar cases have been reported, one by Keith,[13] one by Osgood and Spector,[18] and recently 2 by Hering *et al.*[11]

The purpose of this paper is to describe certain characteristic roentgenologic features of congenital pericardial deficiency with herniation of the left atrial appendage and aid in the differential diagnosis of this abnormal configuration of the cardiac silhouette.

REPORT OF A CASE

R.E.H. was a six year old white male who was admitted to Emory University Hospital for evaluation of a cardiac murmur which had been heard by the patient's pediatrician six months earlier. The patient had a history of easy fatiguability and occasional paleness. Physical examination revealed a Grade IV murmur in the pulmonary area which was continuous through systole and diastole. There was radiation of this murmur into both sides of the neck, the left shoulder and the back. There was no cyanosis or clubbing, and the patient was normally developed and nourished. The family history was noncontributory.

Cardiac fluoroscopy and chest roentgenograms disclosed a heart of normal size. The pulmonary blood flow was slightly increased and the aortic knob was prominent—two findings which suggested the diagnosis of patent ductus arteriosus (Fig. 1, *A* and *B*). In addition to these findings, there was also noted a sharply defined prominence on the left heart border just caudad to the main pulmonary artery segment, which showed active pulsations paradoxical to those in the aorta and pulmonary artery.

At operation, a patent ductus arteriosus was identified, and this was incised and ligated. In addition, the prominence on the left cardiac border was found to be a herniation of the left atrial appendage through a pericardial foramen (Fig. 2). This defect was covered with a flap of mediastinal pleura.

Postoperatively, the patient developed pericarditis with effusion on the seventh day. This was treated with antibiotics, and repeated pericardicentesis. On the fourteenth postoperative day, he was discharged in good condition, and has remained well since.

INCIDENCE

Partial pericardial anomalous defects

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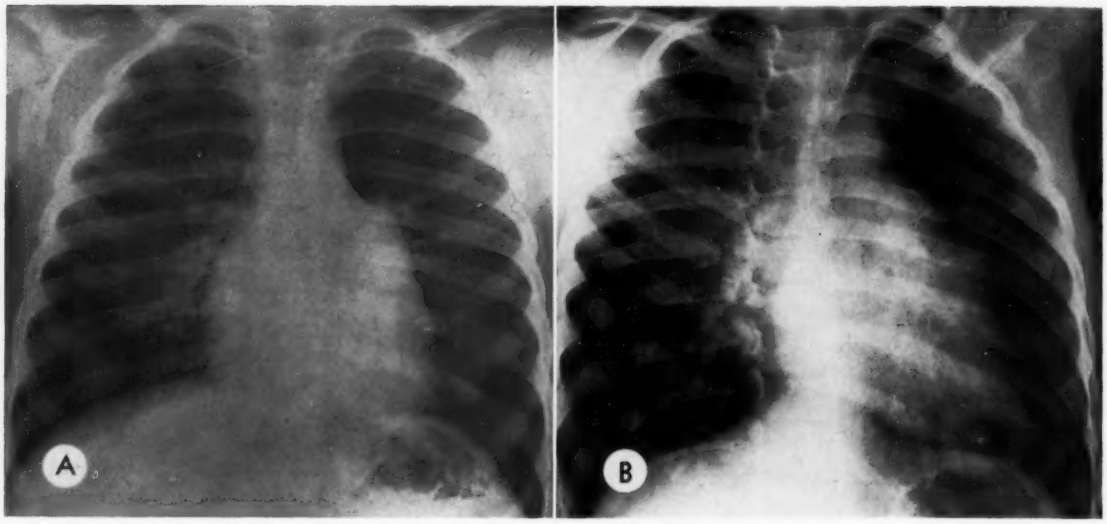

FIG. 1. (*A*) Posteroanterior chest roentgenogram shows a sharply defined and smooth prominence on the left cardiac border just caudad to the main pulmonary artery segment; active pulsations paradoxical to those in the aorta and pulmonary artery were seen during cardiac fluoroscopy. The pulmonary flow appears slightly increased and the aortic knob is somewhat prominent. (*B*) Right anterior oblique roentgenogram of the chest also shows the smooth prominence just caudad to the main pulmonary artery segment.

have been encountered most frequently on the left side. In 108 cases recorded in the literature, the anomaly was left sided in 73 (67 per cent) and bilateral in 3.

Complete or almost complete defects with common pericardial and left pleural cavities are more commonly seen. In 46 cases reported by Southworth and Stevenson,[26] 34 (76 per cent) had a complete defect in the pericardium, and in the remaining cases there was partial absence of this structure, which gave the appearance of a foramen of varying size.

The anomaly appears to be more frequent in males than in females, the ratio being approximately 3:1.

PATHOGENESIS

Though the embryogenesis of pericardial defects in man is not settled, most authors are in agreement that they represent a failure of closure of the pleural pericardial foramen.

Keith,[13] and Rusby and Sellors[23] have suggested that herniation of an abnormal lung bud through the foramen might prevent its closure. Risel[21] differed with these investigators and suggested as a cause an atresia of the pleural pericardial membrane with failure to join the lung roots. McGarry[16] believed that abnormal tension created by the rotation of the developing liver traumatized the pulmonary ridge from which the membrane develops.

Perna[19] and Plaut[20] proposed a vascular atrophy theory based on the hypothesis that premature atrophy of the left duct of Cuvier is causative in producing a deficiency of the blood supply to the pleural pericardial membrane. The latter theory has been generally accepted because it accounts best for the preponderance of pericardial defects on the left side. The possibility that trauma may also play a part in the production of these defects is raised by Moore and Shumacker's[17] recent case, in which there was a past history of a crushing injury to the chest in an automobile accident when the patient was five years of age.

ROENTGEN FINDINGS

The first roentgen diagnosis of pericardial defect was made by Ellis, Leeds, and Himmelstein[9] in 1958. Dahl[8] in 1937 inferred the presence of a communication between the pericardium and the left

pleural space. Following an artificial pneumothorax for treatment of pulmonary tuberculosis in a man twenty years of age, a roentgenogram revealed a pneumopericardium in addition to a left pneumothorax. Kerley[25] mentioned a case of congenital pericardial defect in which the diagnosis was implied after noting pneumopericardium following a diagnostic pneumothorax on the right for investigation of a congenital lung cyst. Jones[12] also observed accidentally a well marked pneumopericardium following a right sided diagnostic pneumothorax for a mediastinal mass.

There are several different types of roentgenologic examinations which can be performed in the investigation of pericardial defects. These will be discussed briefly.

1. *Routine Chest Examination.* In partial defects of the pericardium, the roentgen findings are variable, depending on whether or not there is associated herniation of the heart or lung. If there is a herniation of the heart or lung, the herniated part appears as a mass projecting from the cardiac border. Since the pericardial sac, in the frontal projection, extends between the level of the third through the seventh ribs in their anterior aspect, the mass should be located within this level. The size and the shape of the herniated mass is dependent on the size of the foramen and the herniated part.

In our case, the herniation is best shown in a slight right anterior-oblique view of the chest (Fig. 1*B*). The roentgen findings in the cases reported by Hering *et al.*[11] are identical to those of our case. In the case reported by Rusby and Sellors[23] the roentgen findings are also similar but, in theirs, the mass was due to a lung cyst residing in the pericardial defect. Brea *et al.*[4] observed a smooth projection on the left just below the aortic arch. Case 9 of Jones[12] had a right mediastinal mass due to the presence of a lung cyst associated with a pericardial defect.

In those instances where there is a partial pericardial defect without an associated herniation, there is no demonstrable abnormality in the cardiac silhouette. The cases reported by Dahl[8] and by Venturini and Pesci[28] were of this type.

Fig. 2. Photograph taken at operation indicates the rim of the partial pericardial defect (solid arrows) and the herniated left atrial appendage (broken arrows) through the pericardial defect.

In complete pericardial defect the roentgenographic characteristics are quite different and these are well described by Ellis, Leeds and Himmelstein.[9]

2. *Diagnostic Pneumothorax.* This is a most important diagnostic method of investigation for a congenital pericardial defect; the demonstration of a pneumopericardium following induction of an artificial pneumothorax is diagnostic. Several authors (Dahl,[8] Rusby and Sellors,[23] Kerley,[25] and Jones[12]) have reported the accidental demonstration of communications between the pericardial and the pleural space following the introduction of air into the pleural space.

Ellis *et al.*[9] have recommended, for left pericardial defects, a right posterior ob-

lique roentgenogram of the chest taken with the horizontal beam and the left side down, following introduction of 500 cc. of air into the left pleural space. The absence of a pneumopericardium following pneumothorax does not necessarily rule out the presence of a pericardial defect, since in some cases adhesions might prevent the accumulation of air in the pericardial sac.

3. *Cardiac Fluoroscopy.* Fluoroscopy, especially with an image amplifier, may be helpful to differentiate from a mediastinal tumor; and observation of a paradoxical pulsation to those in the aorta and pulmonary artery might aid in establishing a diagnosis. Our case showed marked pulsation of the mass, and it appeared to be apparently paradoxical to the contraction of the pulmonary artery and the aorta. Rusby and Sellors'[23] case also showed the mass to be pulsatile; however, it was distinct from the aorta.

4. *Angiocardiography.* This procedure may help to rule out other cardiac abnormalities and will give positive information concerning the anatomic location of the herniated part in the case of a partial pericardial defect. It will also permit a differential diagnosis between herniated heart and lung. Kjellberg, Mannheimer, Rudhe and Jonsson,[14] in their textbook on congenital heart disease, reproduced an angiocardiogram showing herniation of the right ventricle through a large left pericardial defect in a six year old girl who also had a patent ductus arteriosus. Recently, Hering *et al.*[11] diagnosed a congenital pericardial defect with herniation of the left atrial appendage preoperatively by angiocardiographic study in a twenty-two year old sergeant of the United States Marine Corps.

DISCUSSION

A review of the literature indicates that in the human subject absence of the pericardium is without significance. Moore and Shumacker[17] carried out total or partial resection of the pericardium in 65 dogs and concluded that in none of these animals was there any indication of impaired cardiac function or dilatation of the heart resulting from the procedure.

The main hazard associated with congenital partial pericardial defect appears to be herniation and incarceration of the heart through the pericardial foramen. In 2 reported cases,[3,27] syncope and death within hours occurred from incarceration and strangulation of the heart by the hernial ring of the pericardium.

A complete absence of the pericardium causes no serious disturbance, and may produce variable cardiac murmurs and mild chronic chest symptoms. The two cases of Ellis, Leeds, and Himmelstein[9] had unexplained chest pain, possibly related to the pericardial defect. Superimposed pulmonary or pleural infection, however, will be dangerous.

Other associated congenital anomalies are also reported in the literature. Kjellberg, Mannheimer, Rudhe and Jonsson,[14] Osgood and Spector,[18] and our present case had patent ductus arteriosus. The case of Rusby and Sellors[23] and 5 cases of Jones[12] had bronchogenic cysts. Brea, Croxatto and De All[4] found an aberrant pulmonary lobe associated with pericardial defect. Moore and Shumacker's[17] case had tricuspid insufficiency of unknown etiology. Ladd's[15] case showed an associated large left diaphragmatic hernia.

Patching of the partial pericardial defect with a flap of mediastinal pleura may prevent herniation of the heart and incarceration by the herniated ring of the pericardium. The partial defect in our case was covered with a flap of mediastinal pleura. Though, postoperatively, this patient developed pericarditis with effusion, he was treated satisfactorily with antibiotics and pericardicentesis. Wide resection of that portion of the pericardium could also prevent herniation and may eliminate immediate postoperative complications.

In addition to the congenital pericardial defect, the acquired herniation as a sequela to intrapericardial surgery, is frequently encountered.

SUMMARY

A case of congenital partial pericardial defect associated with herniation of the left atrial appendage is presented. This patient also had a patent ductus arteriosus.

The literature pertaining to this abnormality is reviewed, and incidence, pathogenesis and roentgen findings are discussed.

Congenital absence of the pericardium is a rare anomaly. In the majority of reported cases, it was found on the left side (67 per cent). Three cases having defects on both sides are reported in the literature. The anomaly is more frequent in males than in females, the ratio being approximately 3:1.

The roentgen findings in this anomaly show certain characteristics. On the routine chest roentgenogram, an abnormal cardiac configuration is seen, there being a smooth projection from the left cardiac border just caudad to the main pulmonary artery segment. On fluoroscopic examination pulsations are noted in the mass, which appear to be paradoxical to those of the pulmonary artery and aorta. The demonstration of pneumopericardium following induction of artificial pneumothorax is diagnostic. Angiocardiographic studies are helpful in determining the anatomic site of the herniation through the pericardial defect.

Repair of the pericardial foramen with mediastinal pleura may prevent herniation and incarceration of the heart. It is possible, however, that wide resection of that portion of the pericardium may also prevent incarceration and strangulation of the heart.

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ROENTGENOGRAPHIC FEATURES OF ASPLENIA, A TERATOLOGIC SYNDROME OF VISCERAL SYMMETRY*

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CONGENITAL absence of the spleen is often part of a syndrome of congenital anomalies consisting of malformations of the heart, partial situs inversus, symmetric lobulation of the liver and the lungs, anomalies of arteries and veins and persistence of the dorsal mesentery to the duodenum and colon.[10,13,14,15] This is a rare syndrome, but has been reported in the medical literature with increasing frequency in recent years.[1,9,14]

Putschar and Manion[15] reviewed the literature in 1956 and noted that 78 cases of congenital absence of the spleen had been reported; of these 29 cases were associated with malformations of the heart and partial situs inversus, and 20 cases were associated with cardiac malformations without situs inversus. Polhemus and Schafer[14] in 1959 were the first to point out that such congenital anomalies and absence of the spleen have a relationship. An excellent monograph was written by Ivemark[10] in 1955 in which he collected the cases in the literature from the first case of Martin (1826) and added 14 cases of his own. Ivemark[10] noted that congenital asplenia was found only 12 times in 7,032 necropsies at the Boston Children's Hospital; associated anomalies of the heart and great vessels were present in 11 of these instances. He suggested that the syndrome of asplenia associated with malformations should be termed "asplenia, a teratologic syndrome of visceral symmetry." He postulated that the basic lesion of the heart occurred during organogenesis when the spleen should have been in its early formative stage of development.

EMBRYOLOGIC CONSIDERATIONS

To better understand this syndrome, it is pertinent to briefly review the embryology of the spleen. By the 14 mm. (six weeks) stage the spleen can be identified as a projection from the mesogastrium between the pancreas and stomach.[6,17] The splenic anlage first appears as a mesodermal condensation in the dorsal meso gastrium. From this mesogastrium several splenic anlagen differentiate. The fusion of these splenic aggregates usually forms a single normal spleen.

Embryologically, the association of the anomalies can be related to the developmental arrest and malformation initiated during the fifth to seventh week of gestation.[10,14] At this time the splenic primordia develop as noted, the heart separates incompletely into two chambers, the definitive pulmonary lobes are forming and the intestine, previously freely movable within the scope of its restraining mesentery, begins its definitive rotation and attachment.[2,14] Ivemark[10] postulates that the adverse causes which may be responsible for dystrophy of the splenic primordium likewise affect the heart and other organs at this early stage. A tendency towards visceral symmetry as noted in this symdrome and the absence of the spleen, the only unilateral mesenchymal organ of the body, was emphasized by Putschar and Manion,[15] who consider the disturbance to be fundamentally a deviation from the normal development of right and left alaterality, resulting usually in various degrees of bilateral right sidedness. The frequent finding of persistent truncus arteriosus, trans-

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position of the great arteries, pulmonary atresia or stenosis, various anomalies of the atrioventricular canal, especially complete common atrioventricular canal and cor biloculare, has led to the consideration that the cardiac manifestations represent abnormal septation of the conotruncus and abnormal division of the atrioventricular canal.

Approximately 100 cases of this syndrome have now been described.[14] Congenital absence of the spleen is a rare anomaly which, in adults, is usually discovered unexpectedly at operation or necropsy. Most cases are seen in young subjects because associated developmental abnormalities are apt to shorten life. The most frequent of these are cardiac malformations and partial situs inversus of the abdominal organs. These were present separately or together in 49 of the 79 cases reviewed by Putschar and Manion.[15] Because of the serious and complex nature of the cardiac malformations associated with asplenia, only 4 of these 79 patients lived three or more years. The majority of the patients were males. In the vast majority of reported cases the diagnosis was made at autopsy.

MATERIAL

Five patients with complete absence of the spleen have been autopsied at The New York Hospital. These are tabulated in Table I and reported below.

The cardiovascular findings are of particular interest. All 5 patients had cyanotic heart disease due to cor biloculare. Associated cardiovascular abnormalities included a right sided aortic arch, a bilateral superior vena cava, partial situs inversus, pulmonary stenosis and atresia and anomaly of brachiocephalic vessels.

One patient had symmetric lobation of the liver and another a centrally placed liver. Three patients showed abnormal lobation of the lungs.

Partial situs inversus was present in 3 of the 5 patients, confirming the statements [4,8,14] that a partial situs inversus of the abdominal viscera in a patient with cyanotic heart disease and the hematologic abnormalities of asplenia indicate that the

TABLE I

FINDINGS IN 5 CASES OF ASPLENIA AUTOPSIED AT THE NEW YORK HOSPITAL

Case No.	Clinical Data	Cardiovascular Findings	Other Autopsy Findings
I.	White male, aged 4 yr. Cyanosis, congestive failure and repeated infections	Cor biloculare; anomalous origin of brachiocephalic vessels	Malrotation of colon; abnormal lung lobation; absent spleen
II.	White female, aged 3 mo. Cyanosis and congestive failure	Cor biloculare; pulmonary stenosis; bilateral superior vena cava; right aortic arch	Dextroposition of stomach; malrotation of cecum; symmetric lobation of lungs; absent spleen
III.	White female, aged 21 yr. Cyanotic since birth, repeated infections and congestive heart failure	Cor biloculare; right aortic arch; bilateral superior vena cava	Centrally placed liver; partial situs inversus; right sided stomach; absent spleen
IV.	Negro female, aged 2 mo. Cyanosis and dyspnea	Cor biloculare; right aortic arch; dextrocardia	Incomplete situs inversus; bilaterally symmetric liver; right sided stomach; absent spleen
V.	White male, aged 2 da. Cyanosis	Cor biloculare; atresia of pulmonary ostium; patent ductus arteriosus	Symmetric lobation of lungs; absent spleen

heart lesion is of the cor biloculare type. Angiocardiographic studies were performed in 2 patients and showed abnormality compatible with situs inversus plus dextroposition of the aorta in Case I and a left superior vena cava in Case III.

It is of interest to note that there were also 2 cases of hyposplenia in the autopsy files of The New York Hospital. One was associated with anomalies in the cardiovascular system; namely, defects in the interatrial and interventricular septa, right sided aortic arch and anomalous pulmonary veins. The other patient had a coarctation of the aorta of the infantile type and a patent foramen ovale. In addition, Brandt and Liebow[2] noted that similar but less complex anomalies may be found in polysplenia.

REPORT OF CASES

Case I. This male infant was seen at The New York Hospital on March 20, 1955 at the age of three months because of dyspnea and cyanosis. He was the product of a full term normal delivery and the mother's prenatal course was uneventful. He had been essentially well until the onset of an upper respiratory infection two days before admission.

He was noted to be acutely ill and had rapid, irregular respirations. The heart was enlarged almost to the anterior axillary line, a precordial bulge was noted and a thrill was felt to the left of the sternum. There was a systolic murmur, maximum in the third left interspace. He was digitalized and given antibiotics and oxygen. Angiocardiography was performed on April 12, 1955 and showed a single large atrium and a large ventricle with dextroposition of the aorta (Fig. 1). He showed satisfactory response to therapy and was discharged on April 29, 1955.

After discharge the patient had repeated bouts of upper respiratory infection and gained weight slowly. Development was somewhat retarded.

Laboratory studies on January 24, 1956 showed the blood hemoglobin to be 10.5 gm. per cent; white blood cell count 28,000 with 68 per cent lymphocytes, 1 per cent monocytes, 2 per cent basophils, and 29 per cent polymorphonuclear leukocytes. Blood smear showed hypochromia, target cells, polychromatic cells and spherocytes. An electrocardiogram was indicative of right ventricular hypertrophy.

Fig. 1. Case I. Frontal angiocardiogram showing a single large atrium and a single large ventricle with simultaneous filling of the pulmonary arterial circulation and a dextroposed aorta.

On January 26, 1956 pneumoperitoneum (Fig. 2) and laminagraphy of the abdomen confirmed the clinical suspicion of an absent spleen. On February 19,1956 he developed a left otitis media and thereafter he continued to have recurrent ear infections. Cardiac catheterization was carried out on March 22, 1956 and showed a 75 mm. Hg pressure gradient from right ventricle to pulmonary artery. The "right" ventricular systolic pressure was identical to the brachial artery systolic pressure. The catheter entered a superior right pulmonary vein from the "right" atrium.

Chest roentgenograms showed a large heart shadow which increased in size between January 23, 1956 (Fig. 3*A*) and October 10, 1957 (Fig. 3*B*). Upward tilting of the apex, a right sided aortic arch, a concave pulmonary artery segment, diminished pulmonary vascularity, symmetry of the major bronchi and a bifid right fourth rib were also demonstrated.

He subsequently had three hospital admissions for pneumonia and died on October 9, 1959. Autopsy specimens showed cor biloculare (failure of the interauricular and interventricular septa to develop). The heart and lungs together weighed 585 gm. (normal weight 225 gm.). The superior and inferior vena cava and the pulmonary veins entered a common auricle which was dilated and hypertrophied. A right

FIG. 2. Case 1. Angiocardiogram in the upright position after pneumoperitoneum showing a normal diaphragm and no evidence of splenic shadow. This was confirmed by multiple projections and laminagraphy.

auricular appendage was present anterolaterally and a left auricular appendage was present posteriorly. A wide muscular band extended from the right lateral wall of the auricle to the posterior base of the valve between the auricle and ventricle (Fig. 4*A*). The valve was 12 cm. in circumference and had three thickened leaflets with thickened cordae tendinae. The medial leaflets had three poorly defined divisions. The wall of the dilated common ventricle was hypertrophied and the endocardial surface was thickened. A common outflow tract led to the aorta anteriorly and the pulmonary artery posteriorly (Fig. 4*B*). The aortic valve was 4.5 cm. in circumference and the sinuses of Valsalva were dilated. The pulmonary artery was 2.5 cm. in circumference.

There was anomalous origin of the vessels arising from the aortic arch. A right subclavian and right common carotid artery arose from the right side of the aortic arch and an innominate artery from the left side. There was abnormal lobation of the lungs. In the left lung

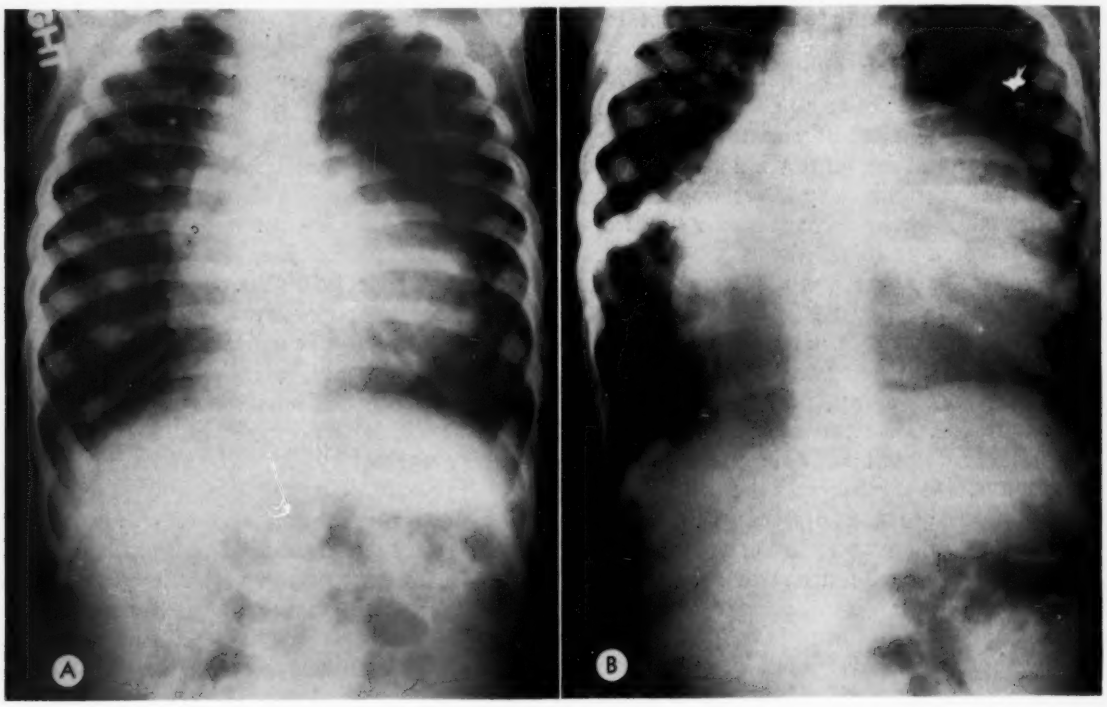

FIG. 3. Case 1. Teleroentgenograms of the chest. (*A*) Examination on January 23, 1956 showing enlargement of the cardiac shadow, upward tilting of the apex, concavity of the pulmonary artery segment and hypovascularity of the lung fields. There is a congenital anomaly of the anterior aspect of the right fourth rib and a right aortic knob. (*B*) Examination on October 10, 1957 showing increase in the size of the cardiac shadow. There is symmetry of the right and left bronchial tree.

three secondary bronchi and three main lobes were present. A small lobe was attached to the left apex and two extra lobes adjoined the left lower lobe. In the right lung, a small lobe was attached to the right apex and an extra lobe adjoined the right lower lobe.

The spleen was absent. There was acute and chronic bronchitis with bronchiectasis and emphysema. There also was incomplete rotation of the large bowel (cecum mobile). The cecum lay on the left side and the entire large bowel was free in the abdominal cavity; its mesentery was attached to the posterior abdominal wall in the midline.

Case II. This three month old white girl was the product of a normal full term delivery following an uneventful antenatal course. She was noted to have intermittent cyanotic attacks and a heart murmur and was admitted for study.

Fig. 5. Case II. Teleroentgenogram of a three month old female showing an enlarged heart shadow, a widened superior mediastinum, clear lung fields and a right sided stomach.

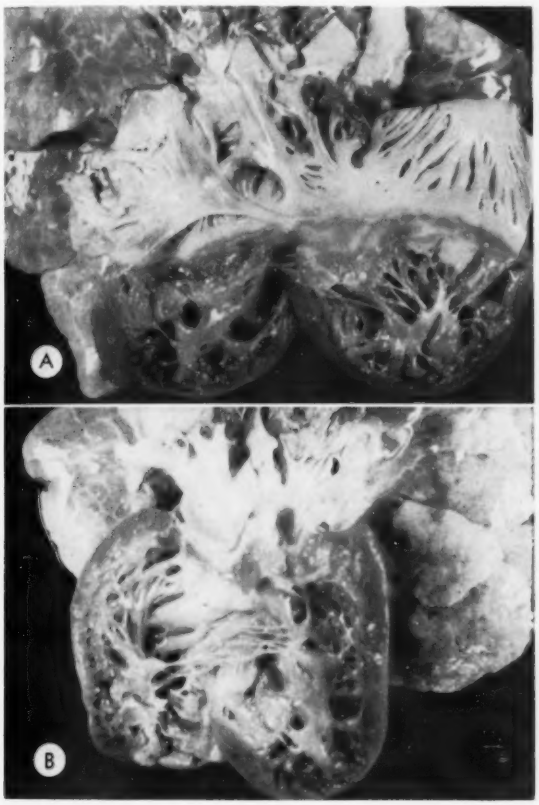

Fig. 4. Case I. Autopsy specimens showing cor biloculare. (*A*) A common auricle and a common ventricle are clearly seen. Note the muscular band extending from the right lateral wall of the auricle to the posterior base of the valve between the auricle and ventricle. (*B*) The pulmonary artery and aorta arise from a common ventricular outflow tract.

A chest roentgenogram (Fig. 5) showed a large heart with a wide superior mediastinum. A straight left border of the mediastinal shadow indicated a bilateral superior vena cava. Lung fields showed diminished vascularity. The right sided stomach shadow indicated partial situs inversus.

Physical examination disclosed a well developed cyanotic white infant. There was tachycardia and a systolic high pitched murmur loudest in the second and third intercostal space over the sternum. No thrill was felt. The abdomen was soft and slightly protuberant with the liver edge 2 cm. below the right costal margin.

Laboratory studies showed a blood hemoglobin of 16 gm. per cent; the white blood cell count was 12,800 with 51 per cent lymphocytes, 8 per cent monocytes and 41 per cent polymorphonuclear leukocytes. An electrocardiogram showed left axis deviation and left ventricular hypertrophy.

Her cyanotic attacks increased in frequency and severity with gradual deterioration. She died at three months of age.

Autopsy revealed a bilocular heart with incomplete partitioning of the atria, a single ventricle, a common atrioventricular canal, pulmonic stenosis, bilateral superior vena cava and a right aortic arch (Fig. 6 *A*).

The heart was moderately enlarged. A right superior vena cava and the inferior vena cava entered the right portion of the atrium. The

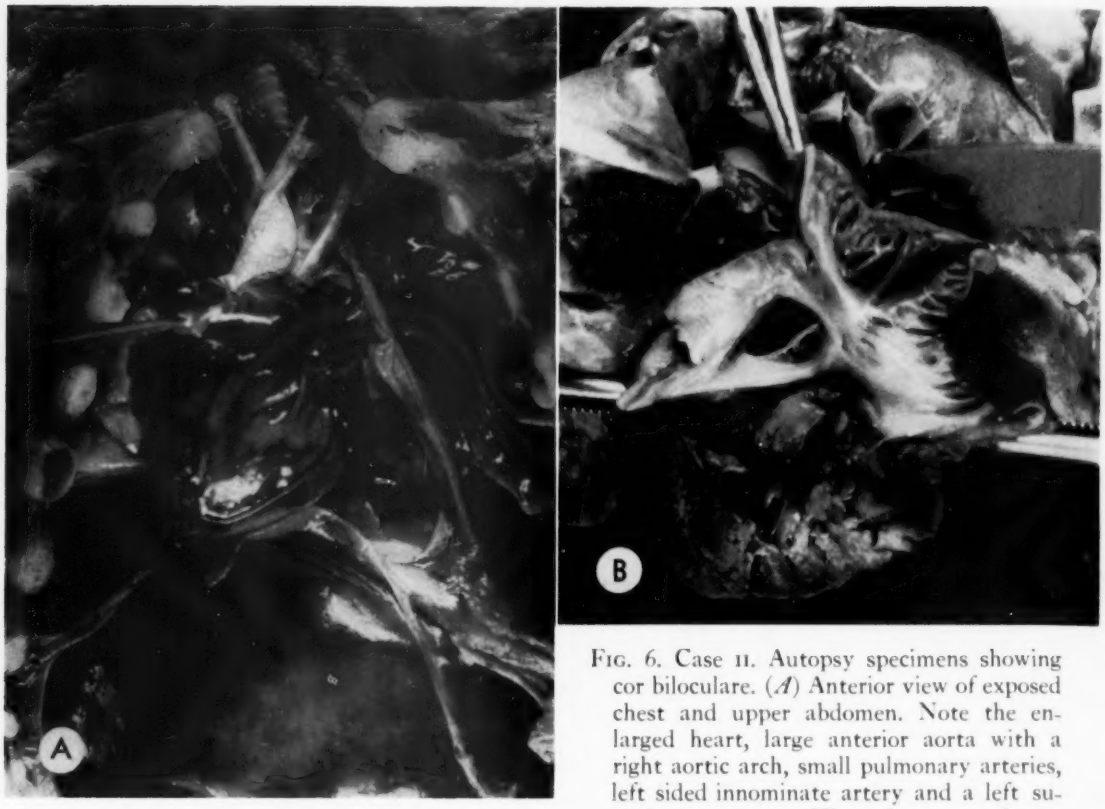

FIG. 6. Case II. Autopsy specimens showing cor biloculare. (*A*) Anterior view of exposed chest and upper abdomen. Note the enlarged heart, large anterior aorta with a right aortic arch, small pulmonary arteries, left sided innominate artery and a left superior vena cava. The spleen was absent. (*B*) Heart opened to show incomplete septation of the atria and a large, hypertrophied single ventricle. There is a common atrioventricular valve with four leaflets.

pulmonary veins and a left superior vena cava entered the left portion of the atrium. A 1 cm. defect, apparently representing the ostium secundum was evident in the upper portion of the interatrial septum; the inferior portion was absent. A common atrioventricular valve with 4 leaflets was present. There was no interventricular septum, but a large leaflet of the atrioventricular valve divided the ventricle into 2 chambers (Fig. 6 *B*). One chamber communicated with the atrium; the other communicated with the pulmonary artery and aorta.

The pulmonic valve was stenotic and had two thick small cusps. The aorta was of normal caliber, anterior and to the left of the pulmonary artery. There was a right aortic arch. The innominate artery passed to the left side of the neck, and the right common carotid and subclavian arteries orginated as separate trunks from the arch of the aorta.

Absence of the spleen and dextroposition of the stomach were noted. The entire colon was in the left lower abdomen. There was symmetric lobation of the lungs; each had three lobes.

CASE III. This female was first admitted at the age of twenty on January 19, 1950 with a history of heart trouble all her life beginning with dyspnea and a heart murmur in infancy. She was first noted to be cyanotic at the age of one week. She had been subject to bronchitis and repeated episodes of pneumonia.

She developed a severe pneumonia four years prior to admission and was hospitalized at another hospital. At that time she had severe shortness of breath and ankle swelling. She was digitalized and subsequently was able to continue normal activity until six months before her admission when she again noted increasing shortness of breath and ankle edema.

Examination showed a well developed woman with cyanotic lips. The apex cardiac impulse was in the fifth intercostal space in the left anterior axillary line. There was a systolic thrill, maximal over the sternum. Auscultation revealed a rough and loud systolic murmur over the entire precordium, loudest in the left parasternal area. A soft and blowing diastolic murmur was audible over the precordium, best heard along the sternal border. There was nor-

mal sinus rhythm. She had marked clubbing of her fingers and toes with cyanotic nailbeds.

Laboratory studies showed a blood hemoglobin of 25.5 gm. per cent and a red blood cell count of 7.5 million. Hematocrit was 72 per cent, and the white blood cell count was 9,600 with a normal differential. An electrocardiogram showed a bundle branch block.

A roentgenogram of the upper abdomen (Fig. 7) disclosed dextroposition of the stomach with partial transposition of the liver. A chest roentgenogram (Fig. 8) showed an enlarged heart and normal pulmonary vascularity. Angiocardiograms (Fig. 9, *A* and *B*) revealed a left superior vena cava and a large posterior atrium and ventricle. There was simultaneous filling of a right aortic arch and the pulmonary artery. Cardiac catheterization showed a right superior vena cava and no distinction between the right and left atrium. There was "right" ventricular hypertension.

She did well for two months following discharge but then was re-admitted because of respiratory distress and fever of unknown origin. She died on September 22, 1950.

Autopsy showed multiple congenital anomalies. Cor biloculare with a common outflow chamber, dextroposition of the aorta, and a persistent left superior vena cava were present.

Fig. 7. Case III. A roentgenogram of the lower chest and upper abdomen after barium ingestion showing a right sided stomach and a centrally placed small intestine. Note the central position of the liver and the left dorsal scoliosis.

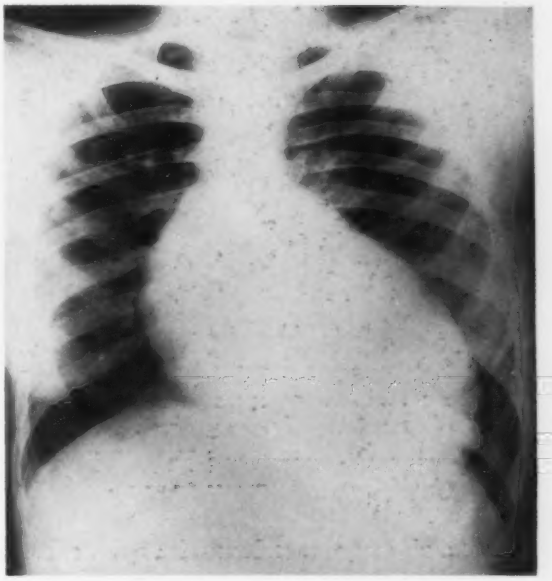

Fig. 8. Case III. Teleroentgenogram of the chest shows an enlarged heart shadow. The superior mediastinum is narrow with straight borders. The lung vascularity is within normal limits.

A single large auricle had a small rudimentary septum hanging from the middle of its anterior wall. Four pulmonary veins emptied into the right side of the auricle, while the inferior vena cava and the two superior venae cavae entered the left side of the chamber. There were two openings leading from the auricle: a well formed tricuspid valve led into a large ventricle, the wall of which was 10 mm. thick. A small slot-like opening at the left inferior position of the auricle suggesting a rudimentary mitral valve but devoid of any cusps led into a small outflow chamber situated in the left upper aspect of the heart. The large ventricle also communicated with the outflow chamber through a cuspless opening situated medially behind the tricuspid valve. Both the aorta and the pulmonary artery originated from this outflow chamber, the aorta anterior to the small pulmonary artery. The pulmonic valve was bicuspid. The aorta had a right sided arch, but was otherwise normal except for moderate atheromatosis. The two coronary arteries arose side by side from the posterior sinus of Valsalva.

There was partial situs inversus. The liver was located centrally in the upper abdomen. The esophagus traversed the right side of the diaphragm and the stomach was on the right side with the duodenum on the left. The spleen was absent.

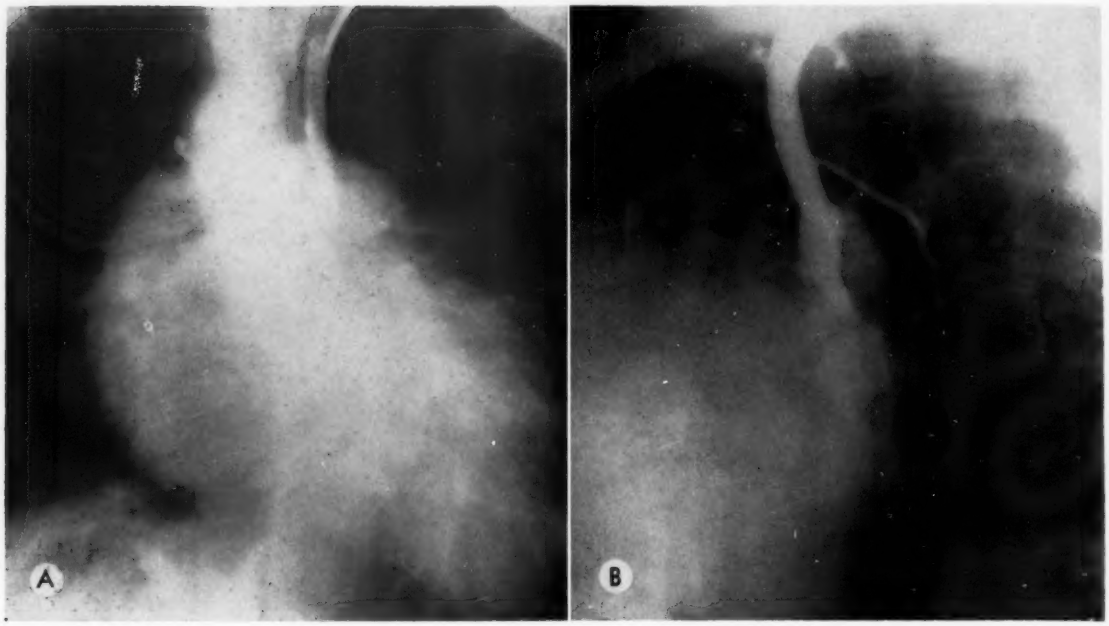

FIG. 9. Case III. (*A* and *B*) Angiocardiograms in frontal and lateral projections showing a left superior vena cava. There is a large posterior atrium and a large ventricle (cor biloculare). A right aortic arch and the pulmonary artery opacified simultaneously.

CASE IV. This two month old Negro female was admitted on December 17, 1949 because of dyspnea and cyanosis. She was born on October 11, 1949 at another hospital and was the 6 pound 11 ounce product of a full term spontaneous delivery. There were no complications during either pregnancy or delivery. The mother was told of no abnormality in the child at the time of discharge.

At about the age of three weeks the baby was examined by her physican and was said to have a heart murmur. The baby's lips were sometimes blue, especially when crying. When two months old the infant developed a "cold" with heavy breathing and an occasional cough. Breathing was rapid and the infant seemed very restless, with several episodes of vomiting.

Examination on admission showed a well developed and well nourished acutely ill infant with dyspnea and flaring alae nasi. The lips, nails and mucous membranes were cyanotic. The lungs were clear to percussion and auscultation. There was a thrill over the right parasternal area in the third and fourth interspaces. There was a loud harsh systolic murmur in the second to fourth intercostal spaces, transmitted over the whole precordium into the neck and the right axilla. The liver edge was 3 cm. below the right costal margin, extending across to the left axillary line, and slightly further below the costal margin on the left. The fingers and toes were cyanotic and clubbed.

Laboratory studies showed a blood hemoglobin of 17 gm. per cent; a red blood cell count of 5,300,000; and a white blood cell of 9,000. An electrocardiogram showed right axis deviation and tracings compatible with a true dextrocardia.

A roentgenogram of the chest and abdomen (Fig. 10) revealed a large heart which nearly filled the thoracic cavity. The liver was bilaterally symmetric, lying transversely across the entire upper half of the abdomen. Fluoroscopy showed dextrocardia and dextroposition of the stomach.

She was placed in an oxygen tent and treated with penicillin and digitalization. She showed no improvement and expired on the third day.

Autopsy showed multiple congenital anomalies with incomplete situs inversus. There was true dextroposition of the heart and aorta, and the stomach, duodenum and pancreas lay on the right side of the peritoneal cavity in the mirror image of their normal positions. The left lobe of the liver was unusually large but the gallbladder lay to the right side of the midline. The cecum and sigmoid were in normal position.

There was cor biloculare: the heart was hugely dilated and filled almost the entire thoracic cavity. It had two chambers with a large single auricle and single ventricle. The pulmonary veins and both venae cavae entered the large atrium in approximately normal position; the aorta and pulmonary artery both arose from the single ventricle. The coronary arteries and the branches of the aortic arch were in normal position. The valve between the two chambers appeared to have four cusps. The ductus arteriosus was completely closed. Histologically, the myocardium was normal, but there was congestion of liver and lungs. No trace of splenic tissue could be identified.

Case v. This male infant was born of an uncomplicated pregnancy on November 2, 1944. Cyanosis was first noted when he was three and one-half hours old and he was given oxygen without significant improvement. Physical examination revealed extreme cyanosis and severe dyspnea. There was slight dullness and diminution of breath sounds in the left upper lobe. The heart rate was rapid and a murmur was not detected.

Fluoroscopy of the chest revealed that the heart was moderately enlarged and globular. The lungs were clear. An electrocardiogram revealed left axis deviation. Laboratory studies showed a hemoglobin of 18.5 gm. per cent; a 5.0 million red blood cell count; and a white blood cell count of 22,700. There were 60 normoblasts per 100 white blood cells.

The baby expired on his second day of life and autopsy showed multiple congenital anomalies. There was cor biloculare with an incomplete fibrous septum between the right and left auricles. The part of the common chamber corresponding to the left auricle was about one-third the size of the right. There was no interventricular septum. Only one valve separated the auricle and ventricle and this had two cusps. A single large papillary muscle arose in the left posterior wall of the ventricle and was inserted at the base of the aorta. The ventricle emptied into the aorta, which was wider than normal. There were three normal aortic cusps and the coronary artery orifices were normally situated. The pulmonary artery was to the left and behind the aorta. Its proximal portion was atretic; distally the lumen was much smaller than that of the aorta. The ductus arteriosus was patent. There were only two arteries originating in the aortic arch, except for the ductus arteriosus. There were three lobes in each lung and congenital absence of the spleen.

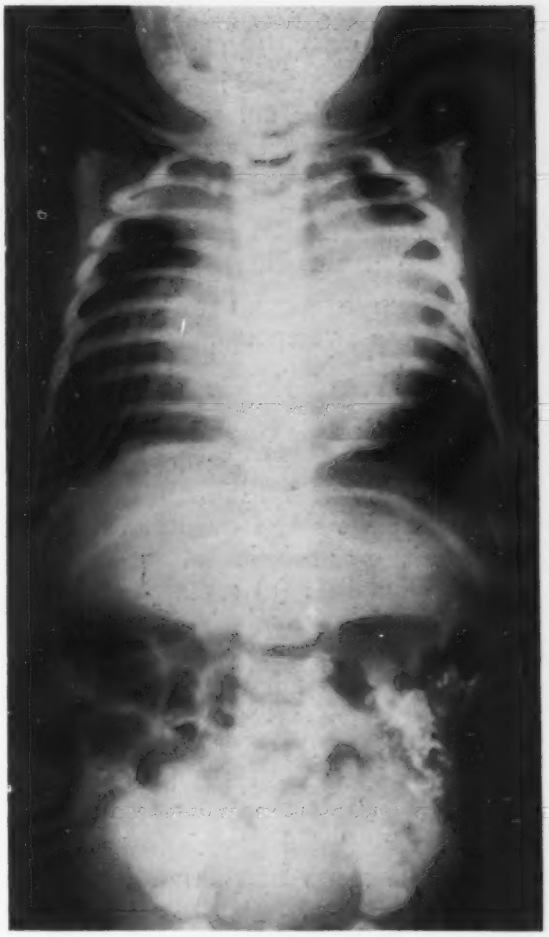

Fig. 10. Case iv. A roentgenogram of the chest and abdomen in a two month old female with asplenia and cor biloculare. There is an enlarged heart with dextrocardia. Note the symmetric liver shadow across the upper abdomen.

Clinical Findings

The first 2 cases of this syndrome to be diagnosed clinically were reported in 1952.[8] The diagnosis was made because of Heinz bodies in the erythrocytes of the peripheral blood in cyanotic infants. Bush and Ainger[4] point out that Heinz bodies are not found invariably in asplenia. However, there may be hematologic abnormalities similar to those found after splenectomy: target cells, decreased osmotic fragility, Howell-Jolly

bodies, transient normoblastemia, siderocytosis and leukocytosis. Thus, the blood picture in splenic agenesis is sufficiently specific to permit the antemortem diagnosis even in the absence of associated anomalies.[4]

The prognosis in this syndrome is extremely poor.[1,10,13,15] A severe anomaly of the heart and great vessels may be predicted and it may be expected that the benefit from surgical correction will be limited.[1] The awareness of agenesis of the spleen is valuable to the cardiovascular surgeon, since the cardiac anomalies often follow a predictable pattern. Aguilar *et al.*[1] reviewed 27 cases of splenic agenesis reported in the literature in addition to 3 of their own cases and were able to show a characteristic association of multiple congenital anomalies: (a) septal defects particularly atrioventricularis communis; (b) anomalous venous return to the heart; (c) pulmonary stenosis or atresia; (d) transposition of the great vessels; (e) accessory lobes of the lungs; (f) partial situs inversus of the abdominal viscera; and (g) abnormal mesenteric attachments.

Thus, all patients with undiagnosed cyanotic heart disease of infancy should have appropiate hematologic studies.[4,5] Abnormalities of the peripheral blood indicative of absence of the spleen are highly suggestive of the complete syndrome being present. Should a partial situs inversus of the abdominal viscera or symmetry of the liver or bronchial tree be evident with the hematologic abnormalities, the associated congenital heart disease is likely to be cor biloculare or a related variant.[4,5,12,14,18,19] Less frequently, there will also be abnormalities of the great vessels. Definitive diagnosis can be aided by roentgenographic studies including angiocardiography and gastrointestinal series.

Splenectomy in the infant before the age of six months is a more hazardous procedure from the standpoint of susceptibility to infection than in older children.[12,16] Serious infections in cyanotic infants, even without other evidence of heart disease, should suggest coexistent asplenia.[12]

ROENTGEN FINDINGS

By definition, the spleen is absent in all cases.[11] Absence of the splenic contour can be difficult to evaluate as the splenic shadow may not be seen in many normal subjects. Brogdon and Crow[3] noted that the lower pole of the spleen may be visualized on the anteroposterior roentgenogram of the abdomen in 44.4 per cent of adults. They feel that nonvisualization is not to be regarded as significant. In our Case 1, pneumoperitoneum and laminagraphy were utilized to document asplenia.

The liver, in this syndrome, is often transposed to the midline or left side of the abdomen with the larger lobe in the left upper quadrant. Ivemark[10] found that the liver was transposed to the left side in 17 of the 69 cases he studied. The liver is frequently symmetric, the left lobe equal to the right in size. This was noted in 31 per cent of the 69 cases of Ivemark.[10] The stomach was transposed to the right upper quadrant in 33 of these cases. Incomplete rotation of the bowel is not uncommon.[10,14,15]

Abnormal lobation of the lungs is frequent in this syndrome. It was evident in 46 of Ivemark's cases. Most commonly, there is symmetric lobation, the lungs being mirror images of each other, with three more or less complete lobes in each lung.[2,10]

The most frequent anomalies in the cardiovascular system are dextrocardia, right aortic arch, anomalies of the atrioventricular region, septal defects, anomalous connections of pulmonary veins and anomalous connection of systemic veins. These may be manifest on routine roentgenograms of the chest. Decreased pulmonary blood flow may also be evident.

Angiocardiography will allow visualization of cardiac chambers and document the size and position of the great vessels, anomalous shunting of the blood stream and anomalous venous return to the heart.[7] Cases of agenesis of the spleen with pulmonary stenosis or atresia with or without transposition of the great arteries may mimic an uncomplicated tetralogy of Fal-

lot.[10] The angiocardiographic findings of cor biloculare are often difficult to interpret. The visualization of a single atrium and a single ventricle on intravenous angiocardiography is compatible with cor biloculare, but other chambers or large septal defects can often not be excluded with certainty. Undoubtedly, selective angiocardiography is preferable in these patients.

SUMMARY

1. Five new cases of asplenia associated with other anomalies are presented with clinical, roentgenographic and autopsy data.

2. The frequency of partial situs inversus, tendency towards symmetry of lung and liver, and the absence of central septa of the heart (cor biloculare) in association with congenital absence of the spleen confirm the value of Ivemark's term: "asplenia, a teratologic syndrome of visceral symmetry."

3. Routine roentgenographic studies are valuable in diagnosis. Partial situs inversus, congenital cyanotic heart disease, symmetry of the bronchial tree and a centrally placed liver should suggest the syndrome. Special studies such as angiocardiography and pneumoperitoneum are presented for their value in antemortem diagnosis.

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EPIDERMOID CYSTS OF THE SPLEEN IN CHILDREN*

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EPIDERMOID cysts of the spleen are rare. They are large fluid-filled masses with a lining of squamous epithelium and are thought to result from developmental rests. The diagnosis may be suspected when gross splenomegaly is encountered in a well child. Roentgen findings include a left upper quadrant mass and displacement or compression of the left kidney. Three cases are presented in which these effects upon the kidney are demonstrated.

REVIEW OF THE LITERATURE

Incidence. Andral, in 1829, wrote the first report of a splenic cyst. By 1956 Posener and Litherland[8] were able to collect 211 splenic cysts of all types from the literature. One of the earliest reports of epidermoid cysts was made by Shawan[10] in 1933. He had 1 case and collected 3 others. Bell,[1] in 1953, found 11 epidermoid cysts in a total of 188 cysts of the spleen which he reviewed. There are numerous other series reported in which a similar incidence of epidermoid cysts is found.[3,6,9]

Classification. There is some variation in the classification of splenic cysts but most authors have followed that of Fowler[3] who divides them into primary or true cysts with a well-defined epithelial or endothelial lining, and secondary or false cysts with no lining.

In the early classifications, true cysts included congenital, traumatic, inflammatory, parasitic and neoplastic forms. The false group included traumatic, degenerative and inflammatory cysts. Cellular metaplasia may account for the presence of a lining in some of the acquired conditions, so that traumatic and inflammatory cysts appear in both categories. The neoplastic group included epidermoids, dermoids, lymphangiomas, and cavernous hemangiomas, although some of these are perhaps more properly developmental aberrations. It is evident that a given case may be difficult to classify under this system. This accounts for the variations in the reported series.

Pathology. Epidermoid cysts are large and may contain from a few hundred to several thousand cubic centimeters of fluid. They are always lined with stratified squamous epithelium which is from five to ten cells thick.[3] The lining is surrounded by a dense hyalinized fibrous tissue. The cysts are usually solitary and are smooth externally. The internal lining may be thrown into folds resembling trabeculations. The fluid varies in color from brown to green and is usually cloudy. There may be fat, cholesterol or calcific debris in the fluid. Dermal structures such as hair follicles and sweat glands are not found. The remainder of the spleen is normal except for pressure atrophy.

Pathogenesis. The true cause for the formation of epidermoid cysts has not been determined. Several theories have been proposed. Shawan[10] and Fowler[3] have suggested that a portion of the celomic cavity capable of forming epidermis is enclosed in the splenic anlage during fetal development. Transformation from splenic mesoderm and from lymphoid endothelium has also been mentioned by these authors. Posener and Litherland[8] further suggest metaplasia following trauma, infarction, hemorrhage, and infection.

CLINICAL MANIFESTATIONS

Although splenic cysts in general are most often seen in the twenty to fifty year age group, epidermoids are found more frequently in the group under twenty years.[5] They are rarely found under five years of age.

The symptoms are minimal. Left upper

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quadrant fullness with vague pain which may radiate to the shoulder, chest, or back may be present. As the mass enlarges, nausea, vomiting, constipation, and dyspnea may appear secondary to displacement of abdominal and thoracic contents. There is frequently a history of either recent or old trauma.

Kidney function may be disturbed by the presence of any large abdominal mass which causes ureteral obstruction, pressure on the kidney, or pressure on the renal artery. Hoffman[4] reported a splenic cyst associated with albuminuria that disappeared following splenectomy. In one of the following case reports, the presenting clinical findings were hypertension and albuminuria.

The physical findings are minimal except for palpation of the mass at examination of the abdomen. Because of their asymptomatic nature, splenic cysts are usually large at the time of discovery. The left upper quadrant mass is usually smooth, nontender, and moves with respiration.

ROENTGEN MANIFESTATIONS

PLAIN ROENTGENOGRAPHY

A large soft tissue mass of water density is seen in the left upper quadrant of the abdomen. The majority of cases seen in childhood do not show visible calcium; however, scattered flecks of calcium may be seen and occasionally the whole mass appears to be calcified. The stomach is displaced to the right. The splenic flexure of the colon is displaced downward and/or to the right. The psoas margin may or may not be obscured. In the lateral projection the mass is seen extending from the anterior wall to the posterior wall. There is frequently a rounded indentation on the anterior wall of the displaced stomach.[11] Contrast studies of the gastrointestinal tract may serve to better delineate these displacements. The left side of the diaphragm may be elevated and left lower lobar pneumonia, atelectasis, and basal pleural effusion have been described. As with any large abdominal mass, there may be limitation of motion of the left side of the diaphragm.

INTRAVENOUS UROGRAPHY

Intravenous urography is of paramount importance in the investigation of an abdominal mass in childhood. The urinary tract may be entirely normal. Frequently, there is either compression or displacement of the left kidney. Displacement is usually downward but it may be upward.[2] Forde *et al.*[2] list 26 cases of displacement of the left kidney by splenic enlargement. In 14, the displacement was downward; in 9, downward and medial; and in 2, upward. Whether displaced or not, the function is good and there is no intrinsic deformity of the calyceal system. Some ureteral obstruction from external pressure may be present with varying degrees of dilatation and persistence of filling. Other cases may show poor filling due to direct pressure or, possibly, due to pressure upon the vascular supply. This may be the mechanism of the hypertension which is seen in cases such as our Case III presented below.

DIFFERENTIAL DIAGNOSIS

Roentgenologically, the differential diagnosis includes other causes of splenic enlargement. Tumors such as lymphangioma and hemangioma are seldom as large. Acquired cysts are impossible to differentiate except by microscopic examination. The history, when definite, may be helpful. Generalized splenic enlargements are usually associated with acute infections or serious diseases such as leukemia and the reticuloses. In these cases the contour of the spleen is maintained with elongation being the most prominent feature. Parasitic cysts of the spleen are diagnosed by their geographic occurrence more than by their roentgen features, although calcification of the wall is a frequent finding.

The differential diagnosis also includes numerous masses outside the spleen. The only significant pancreatic mass in the age group under consideration is the pseudocyst. It is usually not as large and not

situated in as lateral a position and it tends to displace the stomach anteriorly and to the left. Omental and mesenteric cysts are usually movable and rarely are found so far to the left side. Tumors of the left lobe of the liver may closely simulate splenic cysts. They are not so large and frequently the displaced spleen can be seen. Retroperitoneal tumors, including neuroblastoma, usually show their site of origin in the lateral view, especially if skeletal structures are involved. Intrinsic renal tumors almost invariable distort the calyceal pattern and in both renal and pararenal tumors the normal spleen shadow is visible.

The left kidney is not displaced with pancreatic cysts, mesenteric cysts, and tumors of the liver. Neuroblastoma usually displaces the kidney downward when the site of origin is the adrenal gland but the kidney may be displaced upward when the origin is in the sympathetic chain below the kidney. Other retroperitoneal tumors may displace the kidney in any direction according to their site of origin. Retroperitoneal tumors, including neuroblastoma, frequently rotate the kidney as well as displace it, while displacement from splenic enlargement is usually without rotation.

REPORT OF CASES

CASE 1. W.N., an eleven year old boy, was admitted with a complaint of pain in the left hypochondrium. The pain had started about ten days before. It was constant, although occasionally cramping, and was not related to position or eating. There were no other complaints and the past history was negative.

On examination the patient appeared well. The pulse, temperature, and respirations were normal. The blood pressure was 110/55. Physical examination was negative except for the abdomen where there was a 15 by 10 cm. mass in the left upper quadrant extending down to the umbilicus. The mass was smooth, nontender, and fixed, except for motion with respiration. There was no clinical evidence of peritoneal fluid or of peritoneal irritation. Laboratory tests were within normal limits.

Roentgen examination revealed a homogeneous mass of water density in the left upper quadrant extending down to the iliac crest. The margins were not well defined but the mass displaced the colon, small bowel, and stomach to the right side of the abdomen. The margins of the liver, spleen, and psoas muscle were not distinct. Except for displacement, the bowel pattern was normal. Intravenous pyelogram (Fig. 1) revealed good function bilaterally and an anatomically normal right side. The left kidney was displaced upward so that the lower pole was at the level of L-1. There was no intrinsic deformity of the calyceal system. The ureter was well filled. The early studies showed a nephrogram, suggesting partial obstruction of the left ureter.

At laparotomy the mass was found to be a large cyst of the spleen which contained 1,149 cc. of rust colored fluid. It was removed.

Examination of the specimen (Fig. 4 *A*) revealed a large cyst with the wall composed of

FIG. 1. Case 1. Intravenous pyelogram shows the large left upper quadrant mass displacing the stomach and bowel to the right and downward. The left kidney is displaced upward so that the upper pole lies just under the diaphragm. There is slight compression of the left ureter.

hyalinized collagen material lined by stratified squamous epithelium. There were no skin appendages present in the specimen so the pathologic diagnosis was epidermoid cyst of the spleen.

Case II. M.N., an eight year old girl, was admitted with a complaint of swelling in the left side of the abdomen which had been present for one week. There was no pain or complaint of gastrointestinal disturbance. The child had always been in good health. One year previously she had been thrown from a horse but there were no abdominal complaints at that time.

The only abnormal physical finding was a large firm mass occupying the left upper quadrant of the abdomen and measuring 13 by 14 cm. It was smooth and nontender. There was no evidence of peritoneal irritation or free fluid. Temperature, pulse, respirations, and blood pressure were normal. Routine laboratory examinations were normal.

A roentgenogram of the abdomen (Fig. 2) revealed a mass of water density occupying the left upper quadrant displacing the colon downward and the stomach to the right. There was no evidence of free peritoneal fluid and the gas pattern of the bowel was normal except for displacement. The psoas margins were distinct. A definite splenic shadow was not visible. Intravenous urography revealed a normal kidney on the right side. On the left side the calyceal structures were not well filled and the kidney was displaced downward. There was no intrinsic distortion of the calyceal structures. The position of the mass relative to the kidney was such that the incomplete filling could have been the result of direct pressure.

At laparotomy the mass was identified as the spleen. It was cystic and brownish in color. The spleen including the mass was removed.

The specimen (Fig. 4 *B*) measured 20 by 15 by 10 cm. and weighed 1,725 gm. It consisted of a large cyst filled with a turbid greenish-brown fluid. Microscopic examination revealed a fibrous wall lined by stratified squamous epithelium. No accessory dermal structures were found and the diagnosis was epidermoid cyst of the spleen.

Case III. J.B., a thirteen year old boy, was found to have hypertension and albuminuria on a routine physical examination. The patient

Fig. 2. Case II. The left upper quadrant mass has displaced the intestinal gas pattern downward and to the right and the kidney is displaced downward so that it lies over the iliac crest.

was well and had been unusually active athletically. There were no symptoms referable to the cardiovascular or urinary systems.

On admission to the hospital, the temperature and respirations were normal. The blood pressure ranged from 152/104 to 130/72 with most of the systolic readings over 140. The pulse rate ranged from 80 to 114. The remainder of the physical examination was normal except for the finding of a large mass in the left upper quadrant. It moved with respiration and was not tender. Laboratory work demonstrated 25 mg. per 100 mm.^{3} albumin in the urine and 50 mg. per 100 mm.^{3} on a second examination. There were occasional white blood cells, phosphate crystals and granular casts. Blood creatinine, nonprotein nitrogen and serum protein were within normal limits.

Roentgen examination of the abdomen (Fig. 3, *A* and *B*) revealed a large mass of soft tissue density in the left upper quadrant. It displaced

FIG. 3. Case III. (*A*) The left upper quadrant mass has displaced the stomach far to the right and the transverse colon downward. The splenic flexure is situated over the wing of the ilium. The left kidney is displaced slightly laterally and its excretory function appears suppressed by external pressure. (*B*) The lateral roentgenogram shows the indentation of the mass on the anterior margin of the stomach.

the gas-filled colon inferiorly and the stomach to the right. The underlying psoas shadow was visible as was the renal outline. The margin of a normal spleen was not demonstrated. No free fluid was seen. There was a minimal lumbar scoliosis concaved to the left. Intravenous urography showed a normal right kidney. On the left side the collecting system did not fill well but there was no intrinsic deformity and only slight lateral displacement of the kidney. On the lateral roentgenogram the mass was seen to be indenting the anterior wall of the gas-filled stomach.

Incomplete filling of the collecting system on the left side as compared to the good right kidney was quite impressive and was interpreted as indicating pressure of the mass on the kidney. It could, however, have been the result of pressure upon the renal artery. Lumbar aortography was not done.

At laparotomy the left upper quadrant mass was identified as the spleen. It was smooth and reddish-purple in color. After removal of the mass, it was noted that the left kidney appeared somewhat flattened where the mass had been pressing upon it.

Following operation, the blood pressure returned to normal, ranging from 134/70 to 120/64. Repeat urinalysis showed a normal specific gravity, no albumin and only an occasional white blood cell.

The pathologic specimen (Fig. 4 *C*), including spleen and cyst, weighed 3,050 gm. and the cyst contained 2,000 cc. of cloudy brown fluid. The spleen appeared congested. The cyst wall was thick and trabeculated. Microscopic examination showed that the wall was composed of dense fibrous connective tissue lined, for the most part, by a thin layer of stratified squamous epithelium. There were a few small foci of calcified debris. Pathologic diagnosis was epidermoid cyst of the spleen.

SUMMARY

Three children with epidermoid cysts of the spleen are reported. The typical patient is over five years of age and presents with an asymptomatic left upper quadrant mass. The complaints in one case were hypertension and albuminuria, probably due to the pressure of the mass on the kidney.

The roentgen features include the left upper quadrant mass with displacement of the gas-filled stomach and bowel, absence of the normal splenic margin, and displacement of the left kidney, usually downward but occasionally laterally and upward.

The history, physical findings and roentgen examination, when considered together, may be sufficiently characteristic to lead to the correct diagnosis.

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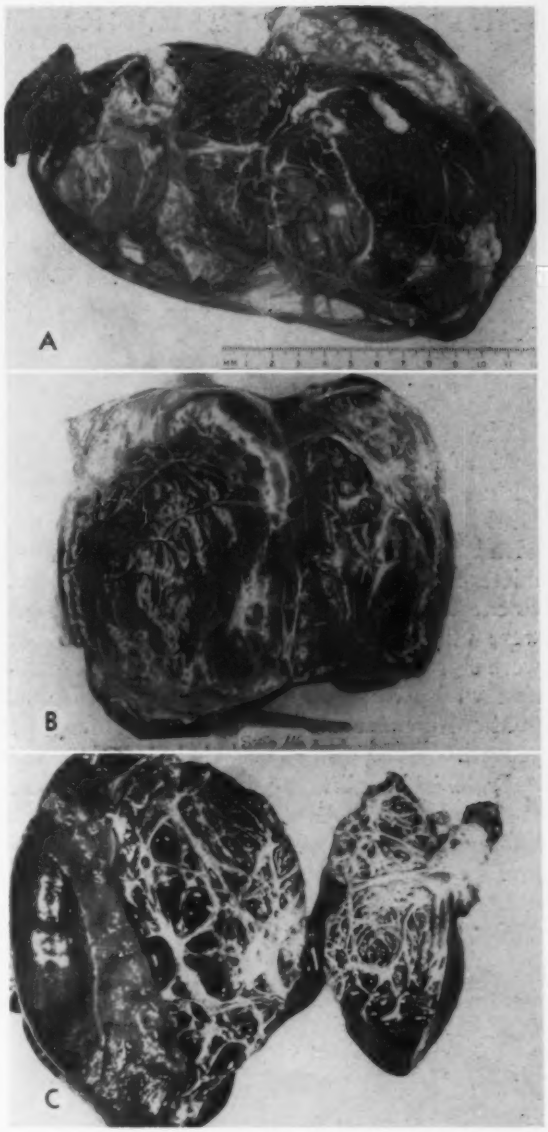

FIG. 4. The cut surgical specimens of (*A*) Case I, (*B*) Case II and (*C*) Case III show the trabeculated cyst wall and demonstrate a remarkable similarity.

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BILATERAL HEMORRHAGIC PSEUDOCYSTS OF THE ADRENAL GLANDS IN A NEWBORN*

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THE purpose of this paper is to describe what is, to our knowledge, the youngest reported patient demonstrating roentgen signs of cystic lesions of the adrenal glands.

REPORT OF A CASE

This white female infant was born June 7, 1960 of a normal spontaneous delivery, with vertex presentation, and cried spontaneously. During the first three days of life, jaundice, with bilirubin reaching 20.3 mg. per cent, intermittent cyanosis and leukocytosis were noted. Roentgenograms of the abdomen and chest were unremarkable at that time. Antibiotics were started and a complete exchange transfusion was performed. Blood and cerebrospinal fluid cultures were negative and the infant improved.

Escherichia coli was cultured from the urine on the ninth day. In the twelfth day of life the infant vomited several times and developed profound shock and cardiac arrest which responded to intracardiac epinephrine and mouth to mouth breathing. A roentgenogram of the abdomen at this time revealed bilateral symmetric rim-like calcifications in both upper quadrants of the abdomen (Fig. 1, *A* and *B*). These were interpreted as most likely representing calcified cystic lesions of the adrenal glands or kidneys. Bilateral masses were now palpable in the upper abdomen. Intravenous pyelography the following day was technically poor and gave no significant information.

At the age of fourteen days, a retrograde pyelogram showed that the calcified masses were in the suprarenal areas, displacing the kidneys downward and distorting the right collecting system (Fig. 2). A lipiodol swallow demonstrated that the stomach and the duodenum were displaced anteriorly.

Exploratory laparotomy was performed on the fifteenth day of life and a cystic lesion containing old blood and measuring 7.5 cm. in diameter was removed from each adrenal gland (Fig. 3).

Microscopically, these cysts showed a

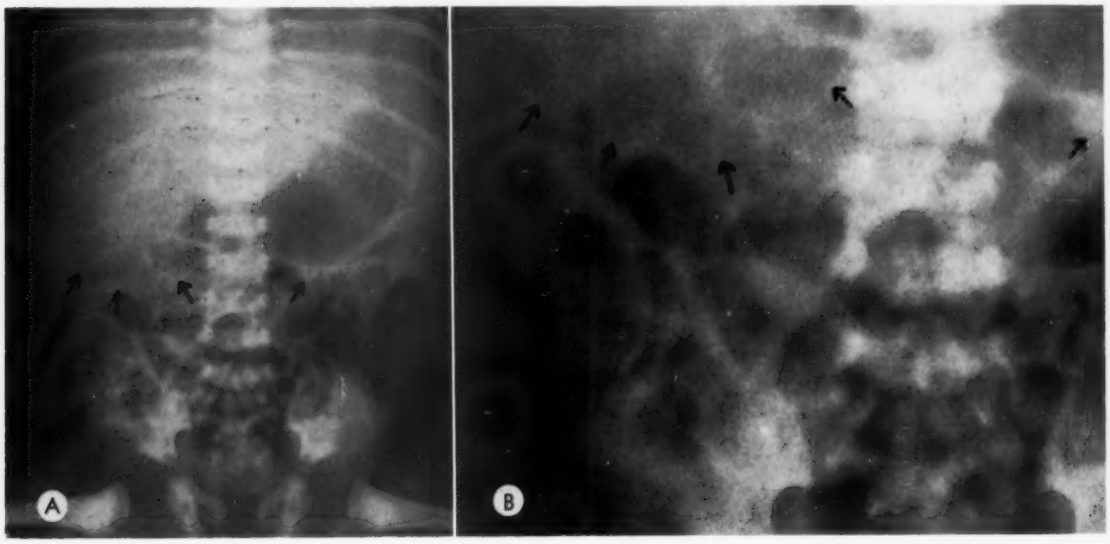

FIG. 1. (*A*) Plain abdominal roentgenogram of the infant at twelve days of age showing rim-like calcific densities (arrows) in both upper abdominal quadrants. (*B*) Detail of *A* showing the rim-like calcification (arrows) in the right upper quadrant.

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centrally located area of infarcted tissue and hemorrhage and a peripheral zone of intact adrenal tissue; between these two areas was a thin layer of calcified material (Fig. 4).

The final diagnosis was hemorrhagic pseudocysts of the adrenal glands. It was felt that the hemorrhage was secondary to infection.

The infant was discharged on August 19, 1960 on adrenal replacement therapy and was doing well. At the age of nine months she was still thriving except for intermittent bacilluria.

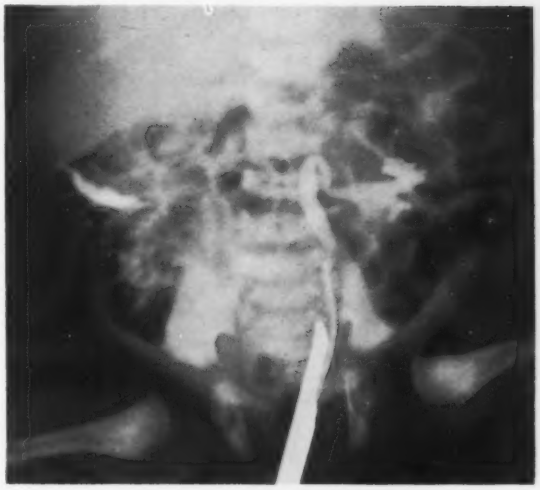

Fig. 2. Retrograde pyelogram of the infant at fourteen days of age showing both kidneys displaced inferiorly and rotated laterally by suprarenal masses. There is some distortion of the collecting system on the right.

DISCUSSION

Adrenal cysts are uncommon. A review of the literature in 1958 disclosed 155 reported cases, found either at surgery or at autopsy, with patient age ranging from the newborn to seventy-six years.[1] In these 155 cases the most common type of cystic lesion encountered was pseudocyst formation incident to adrenal hemorrhage (50 cases).

In the young, adrenal hemorrhage is not rare. It was noted in slightly more than 1 per cent of a series of autopsies performed on infants and children,[33] and it may be unilateral or, more commonly, bilateral.[36] It has been reported in association with birth trauma (including forceful resuscitation),[18,32,33,36] infection,[18,32,33,36] hemorrhagic disease of the newborn,[32,33] physiologic involution,[18,36] regional suppuration with thrombosis of the adrenal vein,[20] burns,[33,36] hemophilia,[36] syphilis,[36] leukemia,[36] and incompatible blood transfusion.[33] Adrenal hemorrhage in the newborn period is most commonly due to trauma at the time of delivery.[32] The hemorrhagic mass may even reach such size as to cause obstruction of the colon from extrinsic pressure.[10]

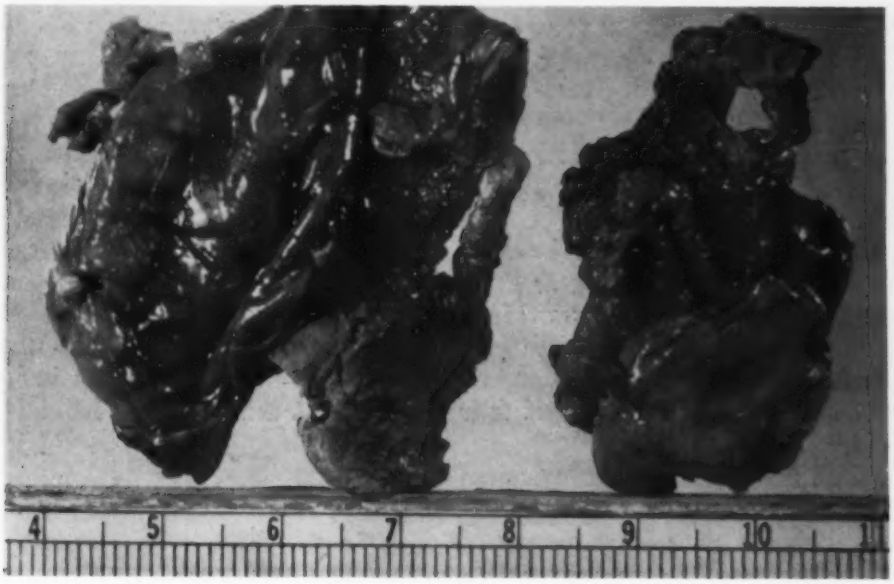

Fig. 3. Photograph of the surgical specimens showing part of each adrenal pseudocyst.

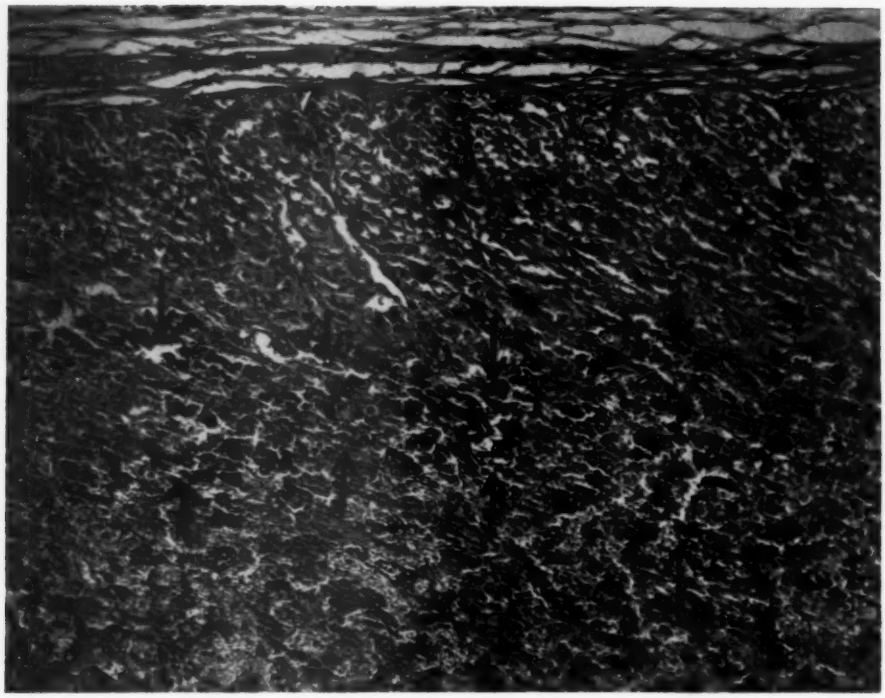

FIG. 4. Photomicrograph of a section of one pseudocyst showing a layer of calcification (arrows) between peripheral, normal adrenal gland tissue (above) and centrally located infarcted tissue and hemorrhage (below) (×100).

Calcification within the adrenal glands may occur following hemorrhage[11,29,34] as well as with tuberculosis,[4,8,11,29,35] ganglioneuroma,[11] neuroblastoma,[11,23] pheochromocytoma,[6,14] carcinoma,[11,31] adenoma,[3] pseudocysts,[21,22,25–28,30,39] generalized xanthomatosis,[22] Niemann-Pick's disease,[28] and *Echinococcus* cysts. The calcification has assumed a rim-like character, however, only in association with cystic lesions of various types, including cystic degeneration within a tumor.

Although the presence of adrenal calcification has been noted at autopsy as early as eight days following adrenal hemorrhage in the newborn,[33] the youngest patient previously reported with roentgenographic evidence of adrenal calcification was four months old.[11]

The mechanism of pathologic calcification has been adequately covered in previous reports,[5,38] as has the clinical picture of adrenal insufficiency.[12,13,15,17,18,24,32,33,36,37]

Calcified cystic lesions of the adrenal glands must be differentiated from other lesions in the abdomen and retroperitoneum which may also show rim-like calcification, such as aneurysms of various abdominal arteries, hepatic and splenic cysts,[28] renal cysts,[16] dermoid and *Echinococcus* cysts,[28] cysts of the mesentery,[19] pancreatic cysts, Wilms's tumor,[22] and renal carcinoma.[9] This is best accomplished by urography. However, with bilateral calcified adrenal cysts, especially in infancy, the diagnosis may be strongly suspected on the basis of the plain roentgenograms alone, since, of the above named lesions, only renal cysts show any tendency to be bilaterally located, and to our knowledge symmetric rim-like calcification has not been reported in this latter condition in early infancy.

SUMMARY

Hemorrhagic pseudocysts of the adrenal glands may show roentgenographically discernible rim-like calcification in a patient

as young as twelve days of age. With bilateral calcification on plain roentgenograms, this diagnosis should be the first consideration and can easily be confirmed by pyelography. This sign should be specifically looked for in any infant exhibiting unexplained gastrointestinal symptoms, collapse, irritability or other signs of adrenal insufficiency.

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VESICOURETERAL REFLUX IN CHILDREN*

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THE purpose of this report is threefold: (1) to re-emphasize that the reflux of urine from the bladder into the ureter is an abnormal occurrence in children or in patients of any age; (2) to outline a simple reliable method for roentgenographic demonstration of reflux; and (3) to briefly review the growing body of literature dealing with vesicoureteral reflux in children.

IS VESICOURETERAL REFLUX ABNORMAL IN CHILDREN?

The varied answers to this question from many physicians, including radiologists, and the paucity of information dealing specifically with reflux in the recent radiologic literature served as stimuli for this report.

Studies in Normal Children. If one were to design a scientific study in an attempt to answer this question, one might start by obtaining cystograms of 100 urologically asymptomatic children with negative urinalyses. Just such a study was performed by Jones and Headstream.[14] They obtained cystograms in 100 children who met the above criteria and found reflux in only 1 child. This child was subsequently found to have a trabeculated bladder with 180 cc. of residual urine due to bladder neck contracture. It is also interesting to note that none of the 100 children developed evidence of urinary infection following cystography. Other investigators have made similar observations prior to and after the above study. Kjellberg *et al.*[15] obtained cystograms of 101 children aged two days to thirteen years who were apparently free of urinary abnormalities and none were found to have vesicoureteral reflux. Keuhnelian examined 26 children who were judged to have normal vesicoureteral junctions and in none of these was reflux observed.[18] Iannaccone and Panzironi[13] studied 50 children aged ten days to six months with no urinary signs or symptoms and found transient reflux in 1, but they were unable to reproduce reflux in the same patient ten days or three and one half months later. Since then, they have been quoted by McGovern *et al.*[18] as not having observed reflux in children without actual or subsequent infection or progressive dilatation. Bunge[2] obtained cystograms of 24 normal children and adults aged nine months to seventy-four years and was unable to demonstrate reflux in these patients. Politano[21] examined over 50 normal children without noting reflux. Campbell,[3] in discussing the cystographic findings in 722 children, states: "Reflux was not observed in any unanesthetized child with a normal bladder."

Earlier reports by Kretschmer[16] and Gibson[9] have given rise to controversy concerning the abnormality of vesicoureteral reflux in children. Kretschmer found reflux in 4 of 11 children, but 1 had cystitis and pyelitis. It is suggested by others[18] that the remaining cases of reflux could have been caused by the irritating qualities of the instilled solutions, resulting in edema about the ureterovesical junction. Gibson demonstrated reflux in 2 of 43 apparently normal children. In this same series 2 other children were found to have vesical diverticula. This would seem to cast some doubt on how many of the 43 apparently normal children actually did have normal urinary tracts.

Thus, the presently available evidence indicates that cystograms rarely, if ever, demonstrate reflux in normal unanesthetized children without other evidence of urinary disease.

Studies in Children with Urinary Dis-

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orders. In contrast to the absence, or extreme rarity, of reflux in normal children is the fact that approximately 12 per cent or more children with urinary disorders have reflux demonstrated on cystograms. St. Martin *et al.*[23] observed reflux in 13.5 per cent of 74 children with urologic signs or symptoms. Forsythe and Whelan[7] found reflux in 13.7 per cent of 445 children with urinary symptoms despite the fact that the complaint was enuresis in 430 of these. Campbell[3] demonstrated reflux in 12 per cent of 722 children with urinary disease. Five hundred symptomatic children twelve years of age or younger were examined by Pasquier *et al.*,[20] and in 13.8 per cent reflux was found. Thirty-five per cent of 152 consecutive symptomatic children examined by McGovern *et al.*[18] had reflux. There were 290 consecutive children with urinary tract infection, but with no evidence of obstruction or neurologic disorder reported by Kjellberg *et al.*[15] and reflux was seen in 34 per cent. Reflux was demonstrated in 34 per cent of our last 50 consecutive children with urinary disorders.

Of even greater significance than the increased incidence of reflux in children with urinary complaints is the observation that when reflux is found there is almost always a demonstrable coexisting or causative urinary disorder. This observation is supported by our studies and by those of others. McGovern *et al.*[18] state that, in their series of 88 children demonstrating reflux, "100% have significant urinary abnormality besides reflux." In Campbell's[3] aforementioned study of the cystograms of 722 children, he did not observe reflux except when other demonstrable uropathy coexisted. In discussing his series of 500 cystograms of children, Pasquier *et al.*[20] state, "In every instance we have been able to demonstrate an adequate cause for the reflux."

PATHOPHYSIOLOGY OF REFLUX

The ureterovesical junction is anatomically constructed to prevent reflux. According to Campbell,[3] "Normally the ureter enters the bladder obliquely for a distance of 5.0 mm. in an infant and 20.0 to 25.0 mm. in an adult, thus forming an oblique valve arrangement with a thin overhanging ureteral meatal lip to prevent backflow of urine." Gruber[10] observed that the percentage of reflux varied inversely with the thickness of the bladder and with the length of the intravesical portion of the ureter. Melick and Naryka[19] have shown with the strain gauge, a highly accurate instrument for measuring intravesical and intraureteral pressures, that, as the bladder is distended with fluid, the pressure in the normal ureter rises and remains higher than the intravesical pressure. From their studies they believe that this is the normal mechanism by which reflux is prevented. They also observed that reflux occurs when the ureteral peristaltic pressure fails to rise sufficiently as the bladder pressure rises. This increase in ureteral pressure may be due in part to the bladder compressing the intramural ureter plus the added factor of ureteral peristaltic pressure. Edwards[6] and Hanafee and Turner[11] observed cineroentgenographically that children with bladder neck obstructions had reflux into atonic ureters. In cases with simple megaureter, active forward and reverse peristalsis was observed. Pasquier *et al.*,[20] in preliminary studies with combined cystograms and cystometrograms, have shown that there is reflux with low bladder volumes and pressures in some children, while in others large volumes and high pressures are necessary before reflux occurs. Briefly stated, there is some type of unidirectional valve mechanism in the intramural portion of the normal ureter. This valve action may be active or passive or both.

Infection. There are many disease states which are able to alter the function of the ureterovesical junction, thereby causing reflux. In the acute phase, infection may temporarily convert the intramural ureter into a semi-rigid tube by surrounding edema and induration. Auer and Seager[1] produced experimental edema at the ureterovesical junction by infiltrating fluid in this area

and were thereby able to produce reflux. Such changes are reversible and reflux may disappear as the infection and edema regress. This may be why the 12 per cent of symptomatic children in whom reflux went undiagnosed in past years have not all had persistent reflux leading to progressive renal damage and death. The unrecognized reflux presumably cleared as the infection subsided with or without therapy. A chronic inflammatory process at the ureterovesical junction may cause fibrosis and scarring, thus changing the distal ureter into a permanently noncollapsible, stiffened tube. Chronic infection might also convert the intramural ureter into an extramural structure, as suggested by Hutch,[12] thereby destroying the valve mechanism which normally would prevent reflux.

Obstruction. Another large group of urinary disorders associated with reflux includes lesions causing obstruction to the outflow of urine such as: posterior urethral valves, median bar, urethral stricture, and other related lesions (Fig. 1, *A*, *B* and *C*). Of 133 children with congenital bladder neck obstruction reported by Uson *et al.*,[26] 67 per cent had reflux. In this group with intravesical obstruction, the changes at the ureterovesical junction are secondary to the obstruction lesion. This group is quite susceptible to urinary infection due to stasis, which probably plays a large part in causing the reflux and vice versa. Eighty-one per cent in the series of Pasquier *et al.*[20] with reflux had infection in addition to bladder neck and intravesical obstruction.

Anomalies. Congenital anomalies such as reduplication of the kidney and ureter or ectopic ureteral implantation are responsible for many cases of reflux (Fig. 2, *A–C*; and 3, *A–E*). Other anomalies in the distal ureter or trigone have been reported.

Neurogenic Disorders. These may produce reflux in some patients (Fig. 4). Swenson *et al.*[25] state: "There is evidence that the parasympathetic system helps to mediate a reflex contraction of the lower ureter during emptying of the bladder. . . . The bladder in some patients with megaloureters is abnormal in function because of a diminution in parasympathetic ganglion cells. The megaloureters are a result of this bladder dysfunction. . . .Certainly most patients with megaloureters have free reflux from the bladder." Perhaps in some cases of megaureter there may be secondary loss of ganglia due to dilatation and atrophy. Other neurologic disorders such as myelomeningocele, faulty innervation of the ureter or bladder, acquired paraplegia, or other types of "neurogenic bladder" may be responsible for the reflux. Only 3 per cent of the patients of Pasquier *et al.*[20] were thought to have neurogenic dysfunction as the cause of the reflux.

The etiology of vesicoureteral reflux is quite varied. Although infection, obstruction or anomalies account for most cases, combinations of these and other causes may interact in the same patient to produce reflux.

DIAGNOSIS

The presenting problem in almost all of our cases of children with reflux was unexplained recurring episodes of pyuria and fever. Flank pain during urination has been mentioned by Campbell[3] as a symptom associated with reflux. Apparently reflux occurs in these children as intravesical pressure rises during micturition. The resulting distention of the upper urinary tract by the refluxed urine produces the flank pain. The ability of a child to pass appreciable volumes of urine when he is allowed to empty his bladder two or three times in sucession suggests the presence of reflux. In these patients, varying amounts of the refluxed urine are passed back into the bladder after it is initially emptied (Fig. 5*E*). Other signs and symptoms are nonspecific for reflux and include almost any urinary complaint.

St. Martin *et al.*[23] have shown that 78.5 per cent of their cases with serious reflux had normal pyelograms. We have made similar observations. Kjellberg *et al.*[15] and

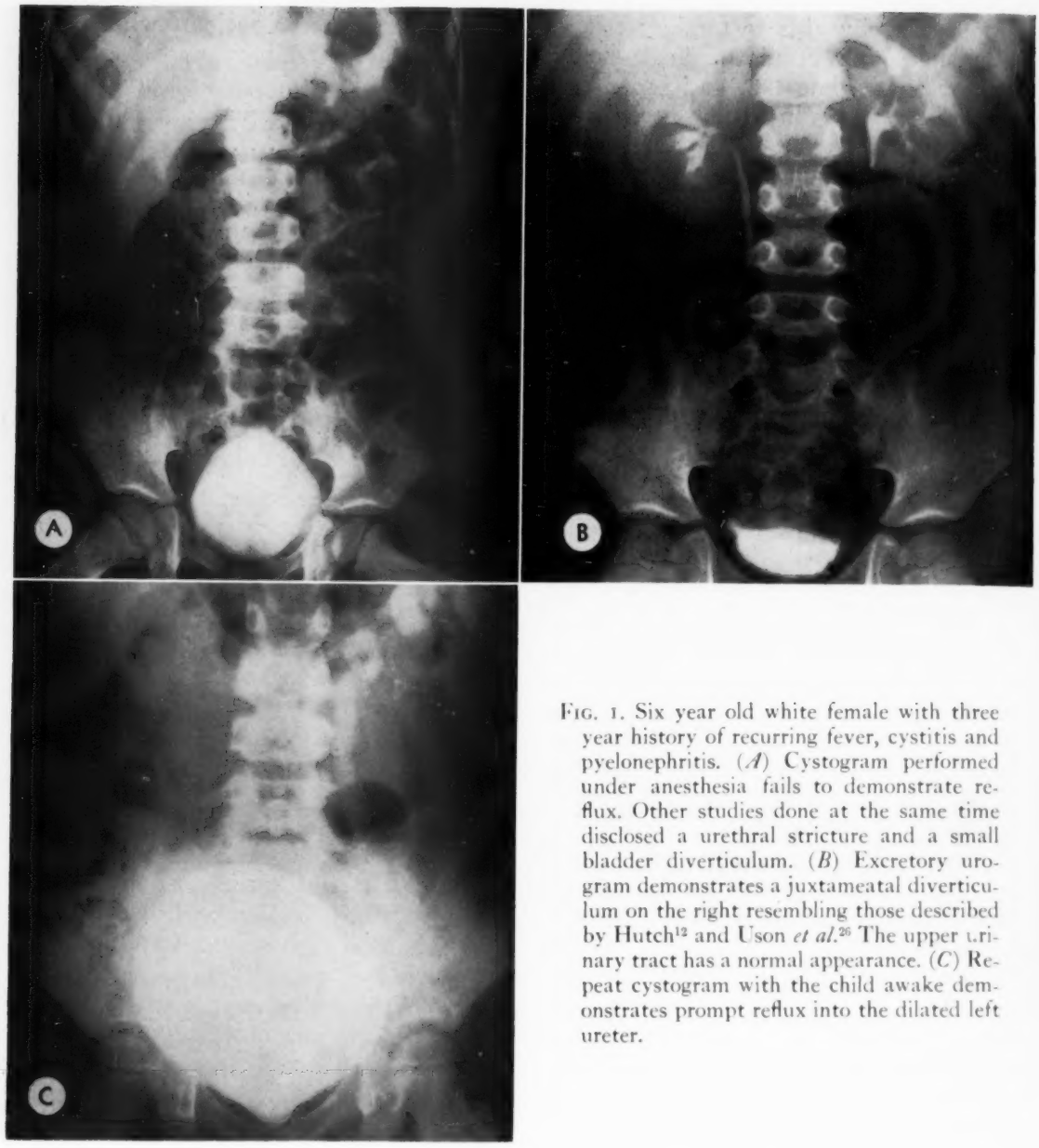

FIG. 1. Six year old white female with three year history of recurring fever, cystitis and pyelonephritis. (*A*) Cystogram performed under anesthesia fails to demonstrate reflux. Other studies done at the same time disclosed a urethral stricture and a small bladder diverticulum. (*B*) Excretory urogram demonstrates a juxtameatal diverticulum on the right resembling those described by Hutch[12] and Uson *et al.*[26] The upper urinary tract has a normal appearance. (*C*) Repeat cystogram with the child awake demonstrates prompt reflux into the dilated left ureter.

Stewart[24] report that reflux cannot be predicted from the cystoscopic appearance of the ureteral oriffice. Thus, we see that diagnostic studies in children with urinary problems are incomplete without a test for reflux (Fig. 5, *A–F*). Only two types of tests are available at present.

One method consists of filling the bladder with a solution containing a small tracer dose of radioactive iodine and then surveying the kidney areas for radioactivity with two continually recording devices. This method as presented by Winter[28] has certain advantages, but the expense and the scarcity of the necessary equipment limit its widespread use.

The second method, cystography, is simple and can be easily performed in any radiology department. There have been a few reports[2,4,5,8,24] dealing with variations

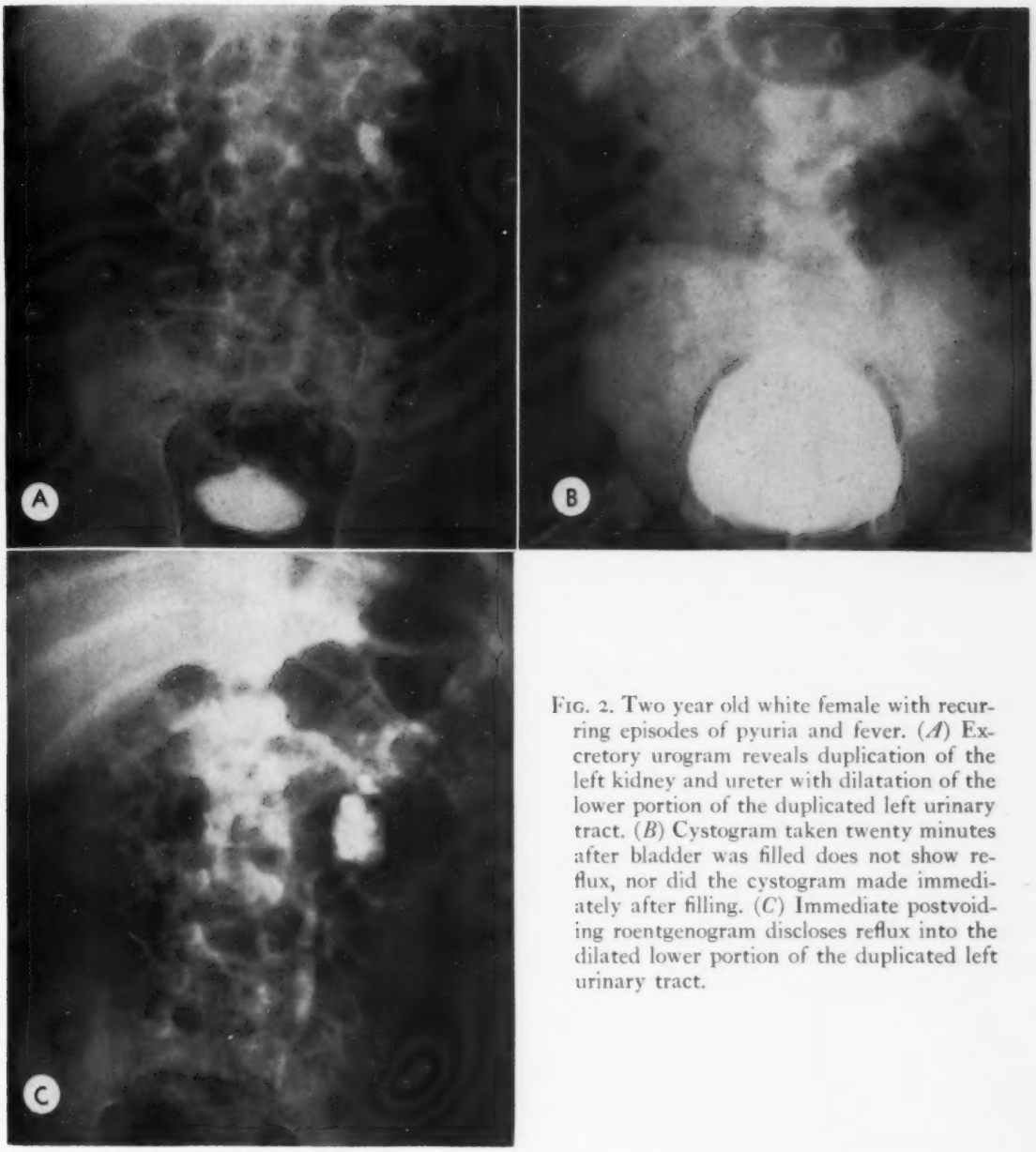

FIG. 2. Two year old white female with recurring episodes of pyuria and fever. (*A*) Excretory urogram reveals duplication of the left kidney and ureter with dilatation of the lower portion of the duplicated left urinary tract. (*B*) Cystogram taken twenty minutes after bladder was filled does not show reflux, nor did the cystogram made immediately after filling. (*C*) Immediate postvoiding roentgenogram discloses reflux into the dilated lower portion of the duplicated left urinary tract.

and refinements in the techniques for best demonstrating reflux. These have definite advantages but the equipment and time required for some of them might tend to discourage their adoption as routine diagnostic procedures. It would seem desirable to emphasize the need for a simple test on all pediatric urologic cases rather than to stress an elaborate one which would only be used on a few children.

PROCEDURE

Certain pitfalls must be avoided in order to prevent false negative or false positive findings of reflux in cystograms of children.

1. The child should not be anesthetized. We have observed 3 children who showed no reflux when cystography was done under general anesthesia but who were found to have marked reflux when these

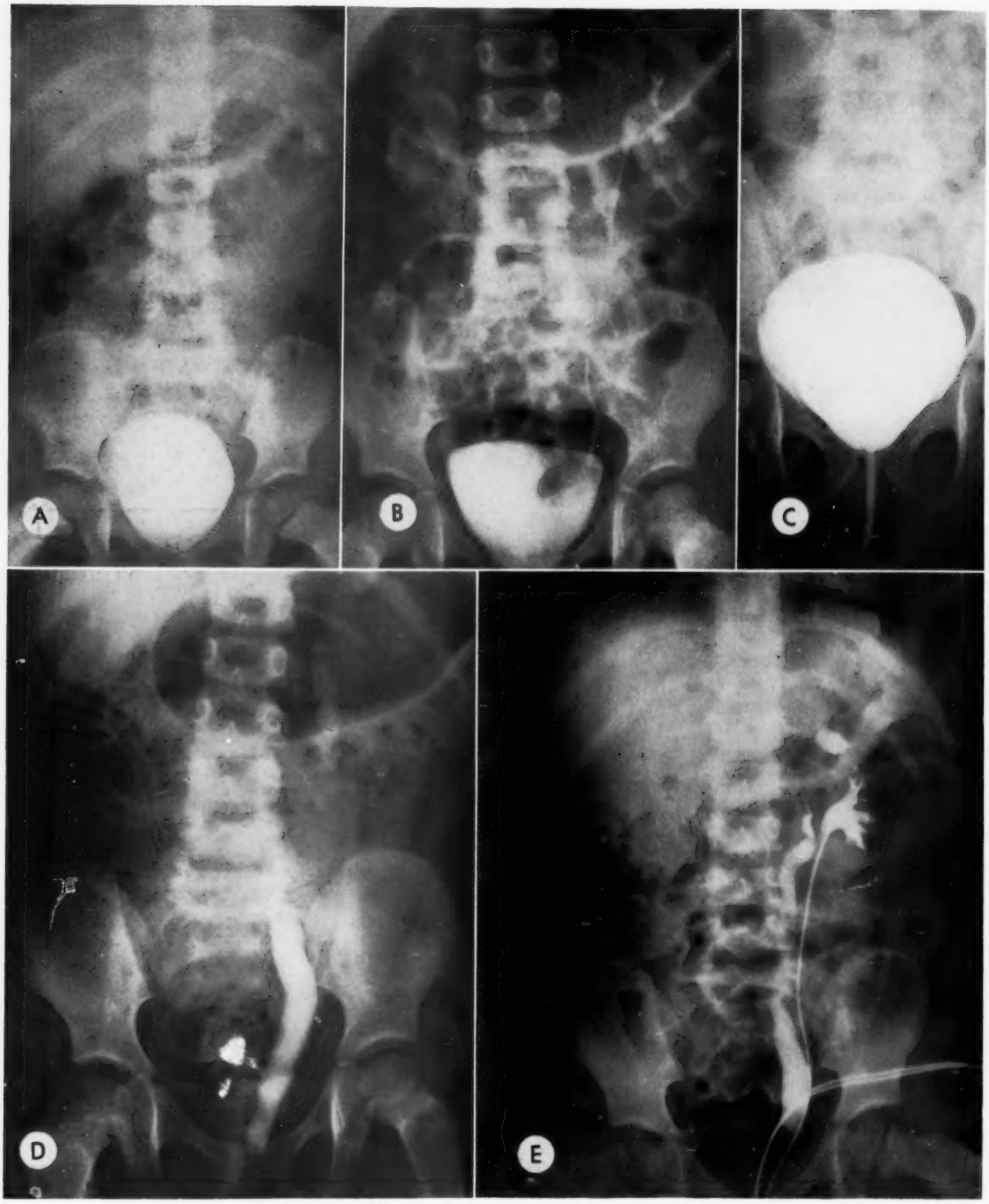

FIG. 3. Three year old white female with fifteen months' history of recurring pyuria and fever. (*A*) Cystogram taken with patient under general anesthesia fails to demonstrate reflux. (*B*) Excretory urogram fails to depict any dilatation or other intrinsic abnormality of the opacified structures. The left kidney is slightly lower than the right, but no opaque medium is seen above it to confirm the presence of a double left kidney. (*C*) Cystogram taken with patient awake. No reflux was seen on immediate or delayed roentgenograms with the bladder filled. (*D*) Immediate postvoiding roentgenogram demonstrates reflux into a dilated ureter from the upper portion of the duplicated left kidney. Note the low midline termination of this ureter. (*E*) On repeat retrograde study, both portions of the duplicated left tract are now depicted. An ectopic ureteral orifice from the dilated ureter was located in the urethra, which explains why this structure was opacified only on the postvoiding cystogram.

studies were repeated with the child awake (Fig. 1, *A–C;* and 3, *A–E*). Conversely, ureteral regurgitation may be seen in an anesthetized child with a normal bladder who demonstrates no reflux on repeat cystograms made while he is awake.

2. A cystogram should be taken immediately after filling the bladder. In some of our patients this was the only roentgenogram which demonstrated reflux.

3. A delayed cystogram should be taken while the bladder remains distended. Most children with reflux will demonstrate it during the first twenty minutes. To lengthen this part of the examination one or two hours or more, as some suggest, might discourage the widespread use of cystography.

4. A voiding or immediate postvoiding cystogram must be taken. In actual practice the voiding cystogram is not always feasible, since most of the patients are too young to cooperate fully. In these cases we have effectively used an immediate postvoiding cystogram. We commonly see reflux only on this one film (Fig. 2 *C;* and 3 *D*). This film also permits visualization of reflux into the distal ureter which might otherwise by obscured by the opacified bladder. St. Martin *et al.*[23] were able to increase their diagnostic accuracy of reflux 50 per cent by utilizing the postvoiding cystogram. If there is any delay in obtaining a postvoiding cystogram, a false negative finding will result, because the ureter will have emptied the refluxed opaque medium back into the bladder (Fig. 5*E*) and this will be misinterpreted as residual urine.

5. Always perform cystography first so that opaque media from excretory or retrograde pyelography will not obscure or be confused with reflux.

6. Use a meticulously aseptic technique when performing the catheterization.

7. Do not use irritating solutions, since the resulting edema may cause reflux.

8. Do not overdistend the bladder. Allow the bladder to drain completely through the catheter before instilling the opaque medium.

Fig. 4. Three year old white female who had had repeated urinary infections since the age of seven months. She also had partial paralysis of the lower extremities and clubbed feet and was later found to have an extradural lipoma in the lumbosacral canal. This cystogram reveals a deformed, contracted bladder and prompt bilateral reflux into a grossly dilated upper urinary tract.

9. Obtain repeat cystograms on children with persistent unexplained urinary infection if reflux is not demonstrated on the first examination, since, in some patients reflux is an elusive phenomenon.

10. Careful attention should be paid to roentgenographic technique in order to minimize motion and other factors which might obscure minimal reflux. Always obtain a preliminary roentgenogram so that technical factors may be corrected if necessary. Be certain that the kidney and bladder regions are completely included on the film.

TECHNIQUE

Utilizing our errors, made in the past, suggestions in the literature, and the experience gained from our last 85 cystographic examinations, the following technique has been gradually developed for obtaining routine cystograms in children. A routine cystogram series is illustrated in Figure 5, *A–D.*

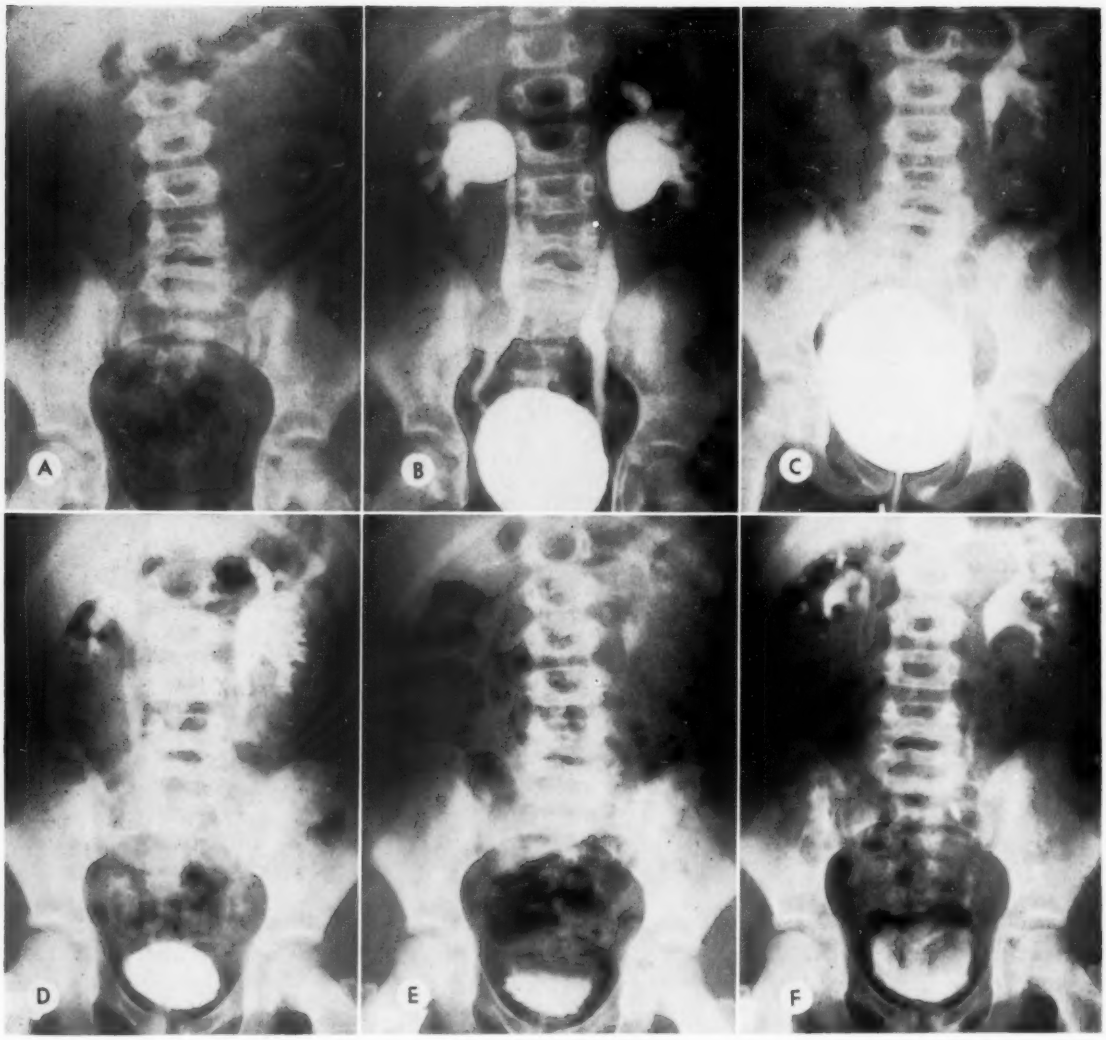

FIG. 5. Four year old white female with a two year history of recurring episodes of fever and pyuria. Subsequently, at the time of bladder neck revision, stenosis of the vesical neck was observed. Figures *A* through *D* constitute the routine cystograms. (*A*) Preliminary scout roentgenogram. (*B*) Cystogram taken immediately after the bladder is filled shows prompt bilateral reflux into slightly dilated ureters, pelves and calices. (*C*) On twenty minute delayed cystogram, some of the refluxed medium is seen to have emptied back into the bladder. (*D*) Immediate postvoiding cystogram reveals that bilateral reflux has again occurred. Residual opaque medium remains in the bladder. (*E*) A second postvoiding cystogram discloses that all the refluxed medium on the right and most of it on the left has emptied into the bladder. Pseudoresidual opaque medium is still present in the bladder. This demonstrates two points: double and triple voiding techniques, as suggested for conservative treatment of reflux, are effective methods to help eliminate stasis; and delay in obtaining the postvoiding cystogram may result in failure to demonstrate reflux. (*F*) Excretory urogram taken immediately after the cystogram appears to be normal.

1. A survey roentgenogram of the abdomen is made.

2. Using aseptic technique, a small catheter is inserted into the bladder and taped in place. The bladder is emptied and this urine may be saved for cultures of other studies. A large piston or bulb syringe is then connected to the catheter with a suitable adaptor.

3. Dilute hypaque (30 cc. ampule diluted with sterile water to 120 or 150 cc.) is allowed to flow by gravity from the syringe

which is elevated above the patient to approximately 20 cm. Usually about 75 cc. of fluid is used in less than three minutes. After this, approximately 50 cc. more is injected under slightly increased pressure. If any of the contrast medium leaks around the catheter or if the child complains of discomfort, the injection is stopped and the catheter is clamped. A total of 100 to 150 cc. of the contrast medium is used in the average young child.

4. As soon as the injection is completed, the second exposure is made. This film is processed and inspected. If bilateral reflux has occurred, omit step five.

5. After twenty minutes the third film is exposed.

6. With the film and roentgen-ray tube in place for a fourth exposure, the catheter is withdrawn. This usually initiates micturition and the child is allowed to void into a pan on the roentgen-ray table. After urination is completed, the pan is quickly withdrawn and the fourth exposure is immediately made.

We now routinely adhere to the above method for obtaining cystograms of children. Since the technicians have become accustomed to this technique, the entire examination is usually completed in approximately twenty-five minutes and it entails only a few minutes of the radiologist's time to perform the catheterization and to inspect the films. Over 90 cystograms have been obtained in the past twelve months at Kennestone Hospital. Seventy-seven of these were on 50 children aged seven months to sixteen years. Reflux was demonstrated in 15, or 34 per cent, of the 44 children, 14 of whom were females. In 6 children the reflux was bilateral.

Fig. 6. White male, sixteen years of age, with uremia and advanced damage to ureters and kidneys, bilaterally. Persistent untreated reflux can produce this result. Every effort should be made to diagnose and treat vesicoureteral reflux promptly if changes such as these are to be avoided.

TREATMENT

It is not the purpose of this paper to fully discuss the management of children with vesicoureteral reflux. Emphasis has been placed on the significance of this abnormal finding and how to demonstrate it roentgenographically. Treatment is mentioned for the sake of completeness and to further stimulate the interest of radiologists in this problem.

Briefly stated, the rationale of management is directed toward finding and eliminating not only the reflux, but the fundamental lesion causing reflux, first with conservative measures and then progressing to more radical methods in the persistent cases. Antibiotics or other drug therapy may be tried first. Measures designed to eliminate residual urine may be tried next, such as multiple voidings (Fig. 5*E*) or urethral dilatations. Leuzinger *et al.*[17] report that two-thirds of 190 children with reflux were greatly benefited following conservative therapy. If the problem persists, less conservative measures may be tried, such as transurethral resection, Y-V-plasty, or other surgical modifications of the bladder neck designed to eliminate obstruction. If reflux persists after correct-

ing the underlying abnormality, it is assumed that the changes at the ureterovesical junction are no longer reversible and surgical modification of the ureterovesical junction may then become necessary. Ureteral reimplantation with the creation of a submucosal tunnel, as described by Politano and Leadbetter,[22] has been quite successful in correcting reflux without producing ureteral obstruction. Politano[21] reports one failure and one partial failure in 26 children following this procedure. Vinson *et al.*[27] report that the Hutch type vesicoureteroplasty was 75 per cent successful in correcting reflux in 178 patients. Pasquier *et al.*[20] successfully corrected reflux with the Hutch type procedure in 10 of 11 children. McGovern, Marshall and Paquin,[18] in their excellent monograph dealing with vesicoureteral regurgitation, discussed 20 children who received vesicoureteroplasties and Y-V-plasties of the bladder neck. Twenty-eight refluxing ureters were reimplanted; reflux was seen postoperatively in only 1 patient and this ureter was subsequently reimplanted with no further reflux.

SUMMARY AND CONCLUSIONS

Vesicoureteral reflux rarely, if ever, is observed in the normal child. It is an abnormal occurrence in children, or in patients of any age, usually indicating an underlying urinary tract disorder. Persistent untreated reflux will lead to progressive and irreversible urinary tract damage. There are several causes for reflux. Urinary infection is important not only as a cause, but also as a result of reflux. Most cases are found to have an obstructing lesion at or below the bladder neck. Three fourths of the children with reflux may have normal pyelograms. Every child with an unexplained recurring urinary problem deserves a complete urologic evaluation which should include properly performed cystography. If the radiologist or urologist routinely obtains cystograms of these patients, his efforts will be rewarded with the demonstration of reflux in 12 per cent or more of them, and with the knowlege that many of these children will be spared the ravages of progressive renal damage (Fig. 6).

Therapy is directed toward eliminating the fundamental lesion and the reflux. Conservative therapy is tried first, and less conservative measures may be necessary in the persistent cases of reflux. Effective therapy is available for many children with vesicoureteral reflux; therefore, the radiologist should make every effort to demonstrate this abnormal finding.

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ADDENDUM

Since this manuscript was submitted, 91 cystograms have been obtained on 78 additional children. Reflux was demonstrated in 21 of these. Thus, in a two year period vesicoureteral reflux has been observed in 36 of the 128 symptomatic childrens' cystograms. In 13 of these 36 children, the reflux was bilateral. Surgical revisions have been performed on 26 of these 49 refluxing ureters which form the basis of a separate report which will appear shortly in the *Journal of the Medical Association of Georgia*.

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INTRALUMINAL CALCIFICATION OF THE INFERIOR VENA CAVA*

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IN THE adult patient, the roentgenographic visualization of intra-abdominal calcification is a frequent finding. The calcification may exist as one or more phleboliths, atherosclerosis of the aorta or its branches, mesenteric lymph node calcification, or a variety of other forms which are readily recognized by roentgenographic means. Calcification within the abdomen of a child, however, is certainly more unusual and often implies a serious condition such as neuroblastoma, teratoma, or, less commonly, an embryoma or Wilms' tumor. Benign forms of calcification, although commonly seen on roentgenograms of the adult abdomen, are infrequent in the pediatric age group. Within the past year we have seen 2 children, who underwent roentgenologic examinations for entirely different reasons, in whom a localized area of intra-abdominal calcification was discovered which at laparotomy was found to lie within the lumen of the inferior vena cava and to be attached to its wall. We have been unable to find similar cases in our teaching file and in a review of the literature.

REPORT OF CASES

CASE 1. J.A.H. (88598) was a six week old white female who was admitted to the hospital because of continued vomiting and poor weight gain. The first hospital admission was at three weeks of age for similar complaints and a diagnosis of hypertrophic pyloric stenosis was made. Laparotomy was performed but the pyloric muscle appeared normal. Gastrointestinal examination had not been performed prior to this surgical procedure. The patient continued to have periodic vomiting and three days after the laparotomy developed diarrhea which was treated successfully with kanamycin and furazone. Prior to institution of chemotherapy, *Klebsiella pneumoniae* and *Shigella A* were cultured from the stool specimen. Because of continued periodic vomiting episodes, roentgenologic examinations of the gastrointestinal tract and urinary tract were performed. Both examinations showed an oval shaped area of calcific density located posterior to the stomach and extrinsic to the kidneys.

The family history was noncontributory and both parents were living and well. The mother's pregnancy was uncomplicated and the delivery and immediate postnatal period were in all respects normal. The patient had been on many different formulas in an attempt to correct the vomiting difficulties but none of these had been successful.

Physical examination showed a well developed, but slightly undernourished baby who was moderately dehydrated. A healed recent abdominal incision was identified, marking the recent laparotomy. There was no evidence of visible abdominal peristaltic waves, nor were there abnormal masses palpated through the abdominal wall. The lower extremities were normal without evidence of edema.

Laboratory studies showed a normal complete blood cell count and urinalysis, and blood chemistries, including sodium, potassium and carbon dioxide determinations, were within normal limits. The VDRL was nonreactive and examination of a stool specimen showed normal trypsin activity.

Roentgen examination of the upper gastrointestinal tract showed no abnormality of the esophagus, stomach or small intestine. However, on all of the roentgenograms there was an oval shaped area of calcific density which measured nearly 3 cm. in length. It was located anterior to the body of L-1 and posterior to the stomach (Fig. 1, *A* and *B*).

In order to investigate the calcification seen on the roentgenograms, an exploratory laparotomy was performed at which time a hard mass was identified within the lumen of the inferior

* From the Departments of Radiology and Pathology, Texas Children's Hospital, Houston, Texas. Presented at the Third Annual Meeting of the Society of Pediatric Radiology, Atlantic City, September 26, 1960.

vena cava. Venotomy was performed and the mass was found to be attached to the anterior wall of the vena cava just above the renal veins. The lesion was removed from its attachment and the venotomy repaired.

Grossly, the specimen was an oval yellow-brown structure with a coarsely granular surface measuring 1.7×0.9×0.3 cm. (Fig. 2*A*). Cut section disclosed an outer irregular calcific capsule with an encapsulated nodule of fibrous tissue. The central portion of this structure was made up of loosely arranged sheets of young stellate fibroblasts and a few thin-walled blood vessels. Hemosiderin laden macrophages were identified within the fibrous tissues. The calcification was present beneath the capsule and was surrounded by a thin compressed layer of mature fibroblasts (Fig. 2*B*). The pathologic impression was that of a calcified organized thrombus from the inferior vena cava.

Fig. 1. Case I. (*A*) Anteroposterior roentgenogram of the right upper quadrant shows an ill-defined area of density overlying the right lateral border of L-1. (*B*) Lateral roentgenogram shows the oval shaped area of calcification to be posterior to the stomach and duodenum.

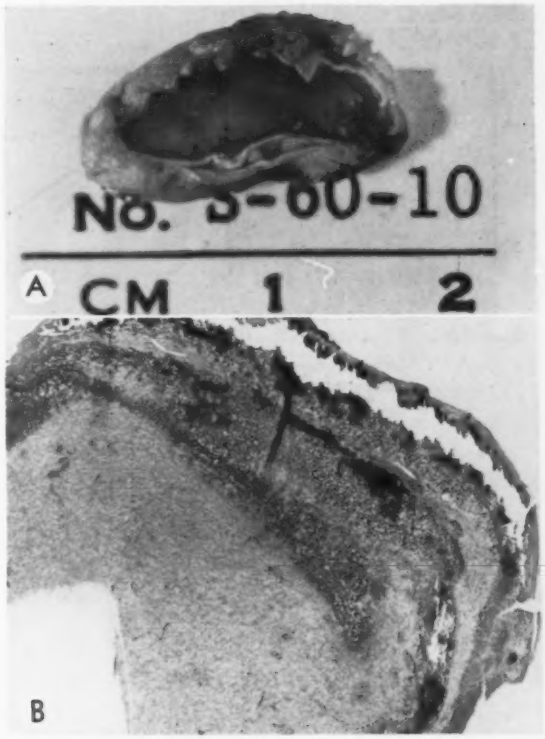

Fig. 2. Case I. (*A*) Gross specimen. (*B*) Histologic section showing features of a calcified organized thrombus.

The patient's recovery following this procedure was uneventful, and, after repeated instructions to the mother in the handling of her baby, the infant stopped vomiting and is no longer a feeding problem.

Case II. P.A.L. (93111) was a four year old white female who was admitted to the hospital for investigation of abdominal pain which had been present intermittently for one month. The discomfort occurred usually in the evening and was located in the left flank and left lower quadrant. In addition, the patient had lost approximately five pounds of weight in the past four weeks. Two days prior to admission, the mother noted that the urine was dark brown in color and on the evening before admission the

patient awakened during the night complaining of severe abdominal pain and this was followed by gross hematuria.

The past history was completely normal other than the usual childhood diseases. Both parents have been in good health and there was no history of maternal illness during gestation.

The abnormal physical findings were limited to the abdomen. There was slight tenderness and spasm over the left flank and left costovertebral angle. A firm, slightly movable, nodular mass was palpated in the left upper quadrant.

Laboratory studies showed a hemoglobin of 12.2 gm. with a hematocrit of 36 mm. The white blood cell count was 10,700 with a normal differential. Urinalysis showed the urine to be dark red in color and loaded with red blood cells. Blood chemistries, consisting of blood urea nitrogen, calcium and phosphorus values, were within normal limits.

Roentgenograms of the abdomen showed a normal distribution of intestinal gas. The right renal shadow was of normal size, but the left kidney appeared enlarged. A triangular shaped area of calcific density having the configuration of a tooth and measuring 1.5 cm. in length was identified to the right of the twelfth dorsal interspace (Fig. 3, *A*, *B* and *C*). Excretory urograms showed nonfunction of the left kidney and retrograde studies showed a mass occupying and distorting the left renal pelvis. The superior and inferior pole calyces were markedly dilated, with the remaining portions of the kidney apparently occupied by a large renal neoplasm. Because of the tooth-like area of calcification, retroperitoneal teratoma with invasion of the kidney was suspected.

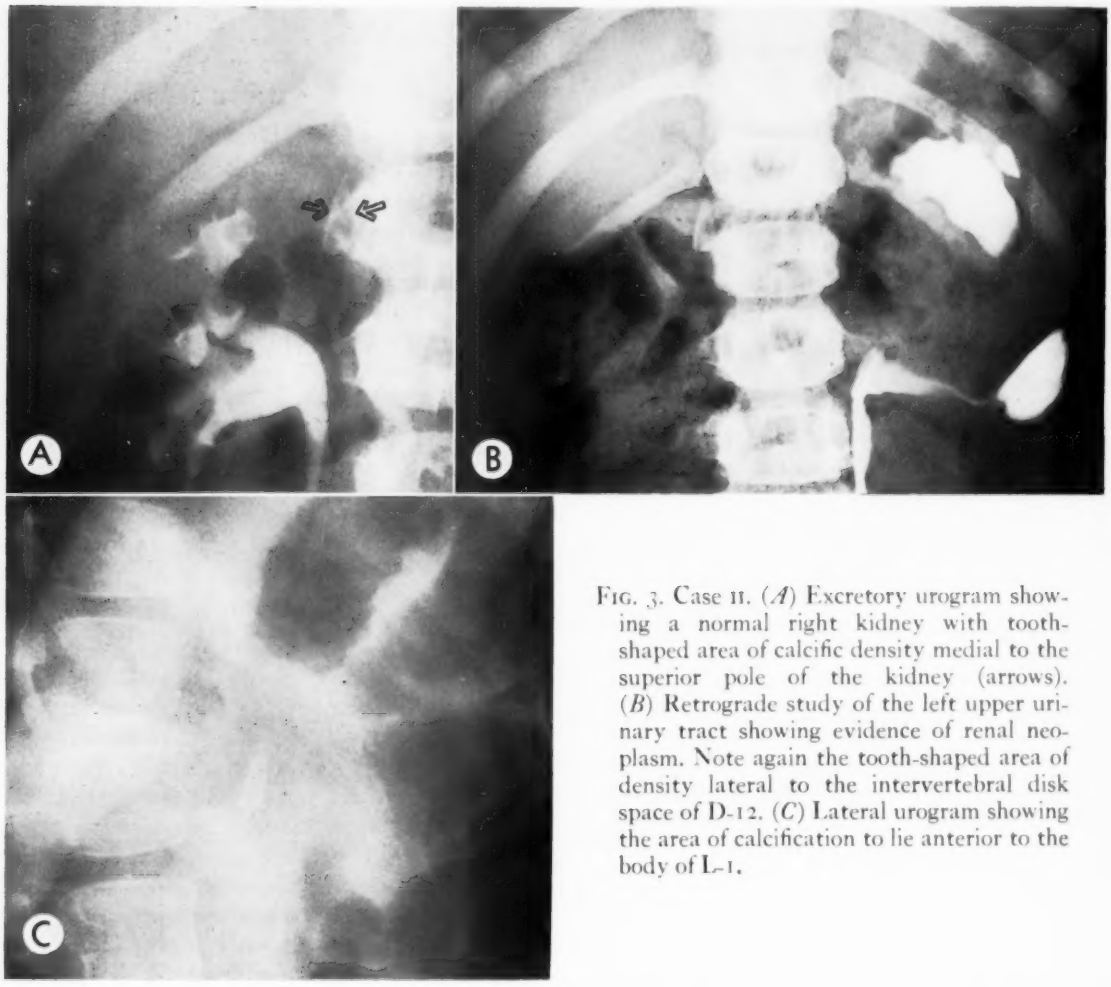

FIG. 3. Case 11. (*A*) Excretory urogram showing a normal right kidney with tooth-shaped area of calcific density medial to the superior pole of the kidney (arrows). (*B*) Retrograde study of the left upper urinary tract showing evidence of renal neoplasm. Note again the tooth-shaped area of density lateral to the intervertebral disk space of D-12. (*C*) Lateral urogram showing the area of calcification to lie anterior to the body of L-1.

Surgical investigation showed a large neoplasm occupying the pelvis of the left kidney which had the gross appearance of a Wilms' tumor. Left nephrectomy was carried out and following this a small firm mass could be palpated in the inferior vena cava, at the area in which the calcific mass was identified on preoperative roentgenograms. Venotomy was performed and the calcific lesion was found to be attached by pedicle to the wall of the vena cava, just above the right renal vein. The lesion was removed without difficulty and the venotomy repaired. The patient made an uneventful recovery and the operative site was treated by external radiation. The patient has remained free of visible neoplasm to the present time, eight months following nephrectomy.

Histologic diagnosis of the renal lesion was Wilms' tumor with vascular and lymphatic invasion. The calcific lesion which was removed from the inferior vena cava was a roughly oval, yellow-brown calcific structure measuring 1.2 ×0.6×0.3 cm. (Fig. 4*A*). The lesion, which had been removed in several fragments, contained a brittle central core. Histologic examination showed the lesion to be an encapsulated amorphous structure which was densely calcified and focally ossified. There were broad areas of edematous connective tissues containing a few fibroblasts, but no evidence of active inflammation (Fig. 4*B*). The histologic diagnosis was organized thrombus of the inferior vena cava.

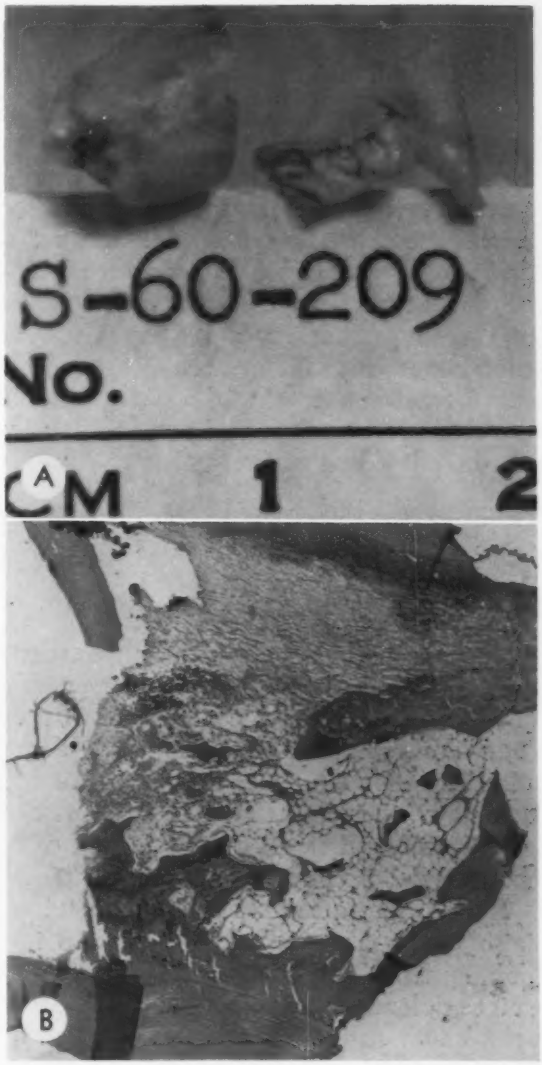

Fig. 4. Case II. (*A*) Gross specimen in fragments. (*B*) Histologic section showing bone formation within the organized thrombus.

DISCUSSION

There are a number of reports in the radiologic literature describing calcification of intra-abdominal veins, as well as calcified thrombi of these structures. This is especially prevalent in patients with Banti's syndrome[3,5,6] and in cases of endophlebitis involving the splenic vein, inferior mesenteric vein, gastroepiploic vein, superior mesenteric vein and portal vein. Li[4] credits Morgagni in 1769 and Baillie in 1793 with reporting calcification involving the inferior vena cava. However, there is no reason to believe that these cases were similar in origin or appearance to the 2 reported here. Although to our knowledge other cases of calcified thrombi affecting the inferior vena cava of children have not been reported, a few have been identified in other institutions.[2,7]

Experimentally, it is recognized that increased pressure within a vein, as well as phlebitis, may lead to thrombosis and this in time may undergo calcification and even later ossification. Neither of the patients described in this report had reason for increase in the pressure of the inferior vena cava such as cirrhosis, portal hypertension or cardiac decompensation. In each case the liver appeared grossly normal at the

time of laparotomy and the spleen was not enlarged. Neither was there a history of phlebitis involving systemic or visceral veins. It is conceivable that in the case of the patient with the suspected pyloric stenosis, the inferior vena cava was locally damaged with resulting thrombosis and calcification. However, the histologic appearance was not that of a recent thrombus but instead suggested that the process had been present for a longer period of time than would have been possible had the thrombosis developed at the time of the recent surgical procedure. In the second case it seems unlikely that the Wilms tumor would have resulted in calcification of the inferior vena cava. There was no evidence of extension of the neoplasm to the vena cava at this point.

Arey[1] has suggested that the thrombus may be secondary to severe dehydration, and, although the first case had a history of recurrent emeses, the infant was never considered to be severely dehydrated. In addition, the histologic appearance of the thrombus suggested that it antedated the period of dehydration. In the second case, there was no history of dehydration.

In addition, attempts to incriminate an embryonic defect have been unsuccessful. Consequently, we are unable to offer an exact etiologic explanation for the calcified vena caval thrombi exhibited by these 2 patients.

One can only postulate as to the eventual result of such a lesion. The possibility of extension of the thrombus with either eventual occlusion of the inferior vena cava or dislodgement of a portion of the thrombus with pulmonary infarction would appear inevitable. Consequently, the surgical removal of these lesions seems justified.

SUMMARY

Two children with calcified masses (probably thrombi) within the inferior vena cava are reported. The etiology is unknown but the possibility of a calcified thrombus of the inferior vena cava should be considered in the differential diagnosis of intra-abdominal calcifications.

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TOTAL ANOMALOUS PULMONARY VENOUS CONNECTION TO THE PORTAL VENOUS SYSTEM: A CAUSE OF PULMONARY VENOUS OBSTRUCTION*

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THE physician confronted with a cyanotic newborn infant must consider the possibility of total anomalous pulmonary venous connection to the portal venous system. This condition leads to death in early infancy. Since surgical correction is theoretically possible, action toward immediate diagnosis is mandatory if surgical salvage of these infants is to be accomplished.

Harris and associates[8] have stressed the value of the thoracic roentgenogram in suggesting the presence of this anomaly. When the thoracic roentgenogram reveals fine stippled reticular pulmonary markings and a normal sized heart, the differential diagnosis in a cyanotic neonate is narrowed to pulmonary parenchymal disease or pulmonary venous obstruction.

Among the several causes of pulmonary venous obstruction is the condition discussed in this paper—total anomalous pulmonary venous connection with a vein of the portal system. This condition may occur alone, or it may be associated with other major cardiac anomalies, with different diagnostic and therapeutic problems in either circumstance. This report will consider only cases that are not associated with other cardiac anomalies. A presentation of the angiocardiographic observations correlated with the pathologic findings in total anomalous pulmonary venous connection to the portal venous system is the major purpose. Angiocardiography was diagnostic in 3 of the 4 patients seen by the authors, and, in retrospect, it could have been the basis of the diagnosis in the fourth patient.

In addition, the clinical, electrocardiographic, and roentgenographic features of our 4 cases will be compared with available data on the 29 other cases we have found in the literature. Description of the attempts at surgical correction of the anomaly in 2 cases will also be given.

CLINICAL REVIEW

A summary of the pertinent data in our 4 cases along with those of 29 cases collected from the literature[1–6,8–11,13,14,16–19] is given in Table 1.

Death occurred in infancy in all cases. Male infants predominated in a ratio of about 3 to 1. A cardiac murmur was infrequently heard. Cyanosis and dyspnea were almost universal. The electrocardiogram revealed right axis deviation and hypertrophy of the right ventricle in every case in which electrocardiographic findings were available.

The literature indicates that roentgenographic studies may lead to a definitive diagnosis of this anomaly. Routine roentgenographic studies reveal the cardiac size to be normal in the large majority of patients. Abnormal pulmonary vascular markings characterized by diffuse, small, irregular densities and described as "reticular markings," "pulmonary edema," and markings "similar to those in neonatal atelectasis" were present in almost all patients

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TABLE I

PERTINENT DATA IN 33 CASES OF TOTAL ANOMALOUS CONNECTION OF THE PULMONARY VEINS TO THE PORTAL VENOUS SYSTEM

Source	Sex	Age at Death	Cyanosis*	Dyspnea*	Swallowing Symptoms*	Cardiac Murmur*	RVH on ECG*	Normal Heart Size*	Reticular Lung Markings*	Angiocardiography*	Surgical Intervention*
Literature (29 cases)	22 M 6 F	2 da. to 3 mo.	22/23	16/17	0/0	5/19	7/7	16/19	17/19	1/29	0/29
Present Authors' Case I	F	4½ mo.	+	+	+	0	+	+‡	+	+	0
Case II	M	5 wk. (PO)	+	+	+	Gr. II† systolic	+	+	+	+	died after surgery
Case III	M	5 wk. (PO)	+	+	+	Gr. I systolic	+	+	+	+	died after surgery
Case IV	M	2 wk.	+	+	+	Gr. II systolic	+	+	+	+	0
Total 33	M 25 F 7	2 da. to 4½ mo.	26/27	20/21	4/4	8/23	11/11	20/21	21/23	5/33	2/33

RVH—Right ventricular hypertrophy; ECG—electrocardiogram; PO—postoperative.
* The first figure indicates those patients with the finding and the second the number in which this finding was considered.
† On the basis of six grades.
‡ Normal at three days of age; cardiomegaly at seven days.

of whom roentgenograms of the lungs were described. Johnson and associates[9] reported the results of venous angiocardiography in one patient in whom contrast medium appeared in the region of the porta hepatis nine seconds after injection. To our knowledge, the present report is the only other description in the literature of the angiocardiographic findings in total anomalous venous connection to the portal venous system.

The following roentgenographic and pathologic findings were observed in our 4 cases.

REPORT OF CASES

CASE 1.*

Roentgenographic Findings. Thoracic roentgenograms were taken in January 1954, of this three day old white female infant during evaluation of cyanosis and dyspnea. Roentgenographic study (Fig. 1*A*) demonstrated that the heart was normal in size and shape. Diffuse fine linear streaks and fine mottling were present in both lungs. A roentgenogram taken four days later revealed cardiac enlargement; furthermore, the fine mottling in the pulmonary fields was accentuated in comparison with that shown at the first examination.

At ten days of age, the patient was subjected to venous angiocardiography. While the patient was in the left anterior oblique position, 4.5 cc. of 35 per cent iodopyracet (diodrast) was injected into the right greater saphenous vein at the ankle. Serial roentgenograms were made at the rate of two per second for five seconds. Review of these roentgenograms showed contrast medium entering the inferior vena cava and progressing to the right atrium and right ventricle and, simultaneously, contrast material filling the left atrium. The pulmonary artery was large and distinct, and it opacified simultaneously with the ascending aorta.

Throughout the remainder of the study the right-sided chambers and the pulmonary artery remained opacified. No opacification of the pulmonary veins or reopacification of the left atrium was observed. A positive diagnosis was not made. Since the patient's condition appeared stable, she was discharged from the hospital.

The patient was re-admitted at three and one-half months of age for re-evaluation of her intensified episodic cyanosis. Thoracic roent-

* Data on this case were included in a previous report by Gott and associates.[7]

genograms revealed moderate cardiomegaly and, as earlier, a fine, lacy, stippled appearance in both pulmonary fields (Fig. 1 *B*). A second angiocardiographic study was performed, 7 cc. of 35 per cent diodrast being injected into the left brachiocephalic vein. Films were exposed at the rate of two per second with the patient positioned in the left anterior oblique. The contrast medium outlined the left innominate vein, the superior vena cava, and the right atrium. Opacification of the large right atrium was followed by simultaneous opacification of the right ventricle and left atrium, then followed simultaneous dense opacification of the aorta which was small and of the pulmonary artery which was large. Again, recirculation of contrast material did not occur, nor did the left side of the heart reopacify. The right atrium, right ventricle, and pulmonary artery remained opacified during the entire study. The patient was discharged on the day of the angiocardiographic study without a definitive diagnosis. One month later, at the age of four and one-half months, the patient suddenly became unconscious and was dead on arrival at the University of Minnesota Hospitals.

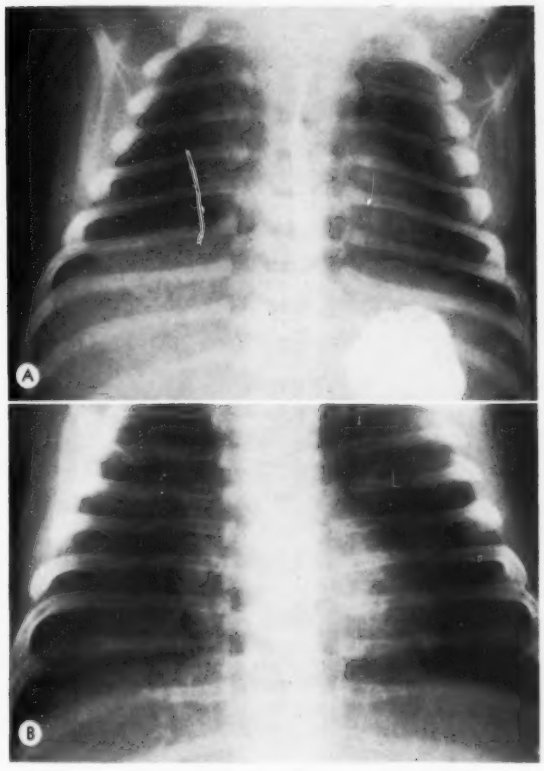

Fig. 1. Case 1. (*A*) Thoracic roentgenogram taken when patient was 3 days old shows normal-sized heart and reticular markings in pulmonary fields. (*B*) Thoracic roentgenogram at 3½ months shows no significant changes from earlier examination.

Fig. 2. Case 1. Frontal photograph of the thoracic and abdominal organs. The heart has been lifted up. The four pulmonary veins converge behind the left atrium to form a common pulmonary vein (C.P.V.). This common pulmonary vein is narrowed at its point of penetration through the esophageal hiatus of the diaphragm. It then becomes dilated and terminates (arrow) in the portal vein (P.) at the confluence of the superior mesenteric vein (M.) and the splenic vein (transected in this specimen). In the thorax the common pulmonary vein is in close association with the esophagus (E.). L.—liver; S.—stomach.

Pathologic Findings. Pertinent findings were restricted to the cardiovascular system. The lungs were expanded and appeared normal grossly. The aorta and pulmonary arteries arose in the normal manner and were normally interrelated. The ductus arteriosus was obliterated. When the heart was retracted upward (Fig. 2), the two pulmonary veins from each lung were observed to join near the midline to form a common trunk. This trunk descended inferiorly, immediately anterior to the esophagus, and it penetrated the diaphragm through the esopha-

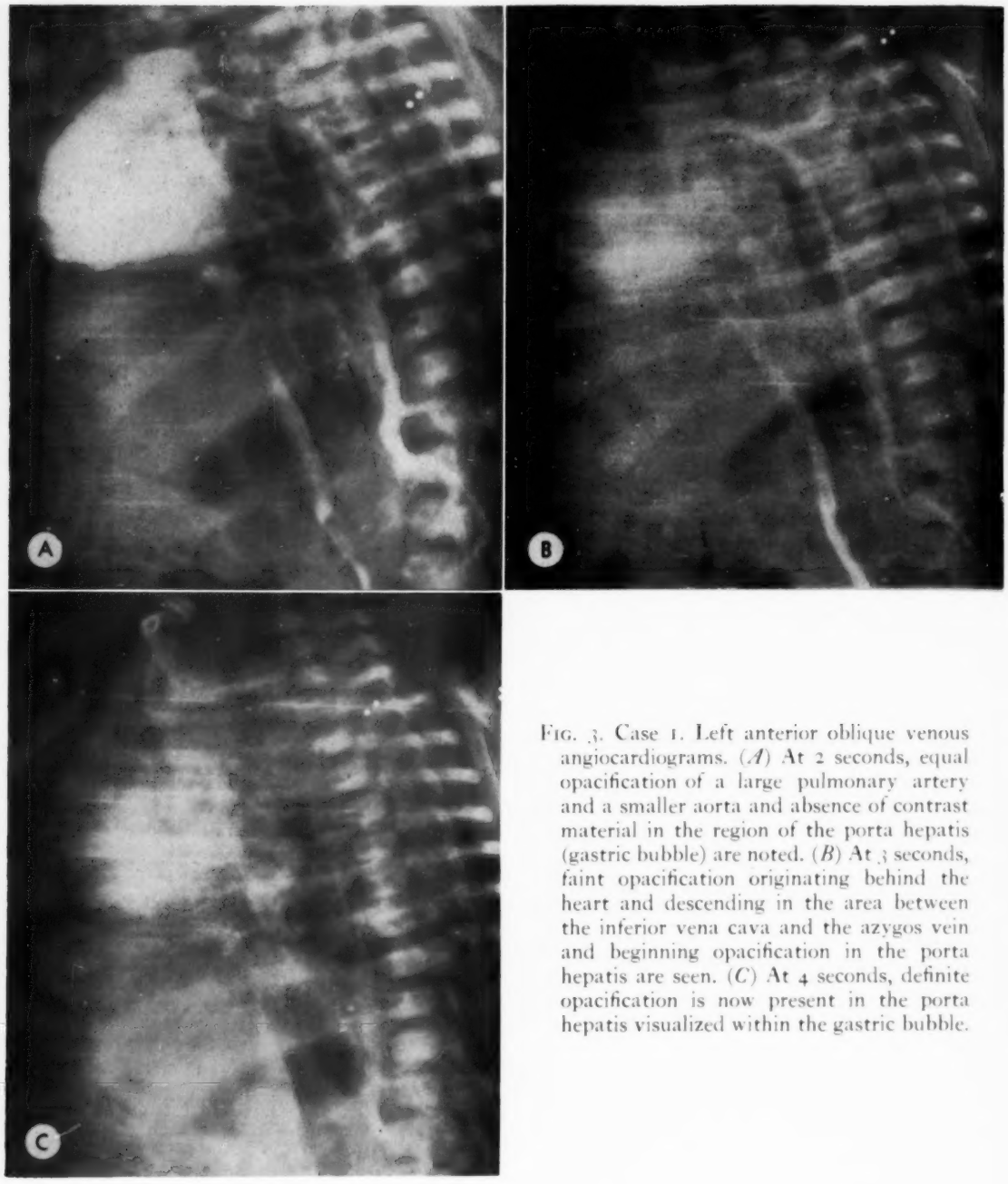

Fig. 3. Case 1. Left anterior oblique venous angiocardiograms. (*A*) At 2 seconds, equal opacification of a large pulmonary artery and a smaller aorta and absence of contrast material in the region of the porta hepatis (gastric bubble) are noted. (*B*) At 3 seconds, faint opacification originating behind the heart and descending in the area between the inferior vena cava and the azygos vein and beginning opacification in the porta hepatis are seen. (*C*) At 4 seconds, definite opacification is now present in the porta hepatis visualized within the gastric bubble.

geal hiatus along with the esophagus. This anomalous common pulmonary vein then joined the portal vein just above the confluence of the splenic and superior mesenteric veins. The anomalous common pulmonary venous trunk was 1 cm. in diameter at its termination at the portal vein. It had a narrow zone which lay in the thorax just above the diaphragm, where the diameter was 4 mm. No pulmonary veins joined the heart directly.

Internal examination of the heart revealed a valvular competent patent foramen ovale with the potential opening measuring 1 × 2 cm. The ventricular septum was intact, and the ventricular cavities as well as the semilunar and atrioventricular valves were of normal size. The left

atrium was small in relation to the right atrium.

It is noteworthy that upon retrospective review of the angiocardiograms obtained when the patient was three days old, we identified faint staining of a vascular channel extending from below the cardiac shadow to a point beneath the diaphragm. In addition, a spherical shadow of contrast medium was observed to lie in the area of the porta hepatis (Fig. 3, *A*, *B* and *C*). This opacification, which occurred late in the examination, had been overlooked during the initial interpretation of the roentgenograms. The shadows noticed retrospectively in this study are thought to represent the lower portion of the anomalous common pulmonary venous channel.

Case II.

Roentgenographic Findings. A four week old white male infant had thoracic roentgenography performed in July, 1959, during evaluation of cyanosis and dyspnea. The roentgenograms demonstrated normal cardiac size and contour. Both pulmonary fields showed a fine, diffuse stippling (Fig. 4). A diagnosis of pulmonary venous obstruction was made.

Three days later venous angiocardiography was performed. Six cubic centimeters of 90 per cent diatrizoic acid (hypaque-M) were injected into the right greater saphenous vein at the ankle while films were being exposed in frontal and lateral projections at the rate of five per second for six seconds. Initially, contrast material outlined the right and left atria. Later, simultaneous dense opacification of the large pulmonary artery and the small aorta occurred (Fig. 5, *A* and *B*). These vessels were in normal position. A patent ductus arteriosus was well visualized. On the late roentgenograms (Fig. 5, *C* and *D*) opacified material appeared in a large midline vascular channel, which extended from the pulmonary hilar regions through the diaphragm into the abdomen. At the distal end of this channel in the region interpreted as that of the porta hepatis was a globular opacified structure measuring 1.5×2 cm. On the basis of these roentgenograms the diagnosis of total anomalous pulmonary venous connection with the portal system was made.

On the seventh hospital day a thoracotomy was performed on the right side. The anomalous pulmonary venous trunk was easily identified in the posterior mediastinum and was followed to its penetration through the diaphragm. When

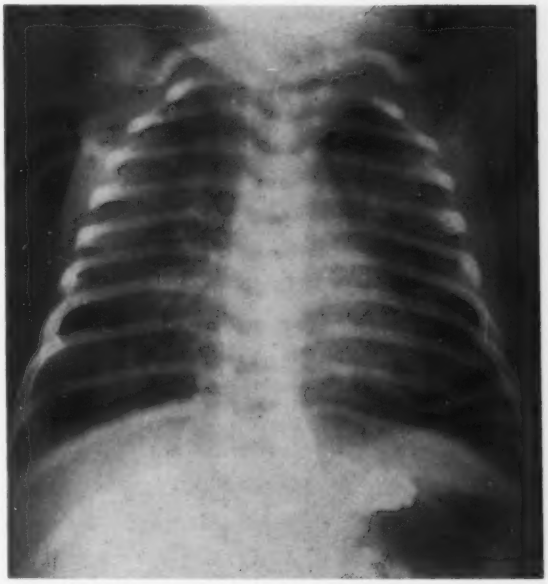

Fig. 4. Case II. Thoracic roentgenogram at 4 weeks shows normal cardiac size and reticular markings in the pulmonary fields.

the pericardium was opened, a small left atrium was identified, with an estimated volume of about 2 cc. Without interruption of venous pathways, the site of convergence of the right pulmonary veins was anastomosed side-to-side to the adjacent wall of the left atrium. The anastomosis was about 1.5 cm. long. At the end of the procedure, the heart stopped, and it was impossible to re-establish a satisfactory beat.

Pathologic Findings. Abnormalities were restricted to the cardiovascular system. The right atrium and right ventricle were dilated and hypertrophied, and the left atrium and left ventricle were somewhat smaller than normal. The aorta and pulmonary artery were normally interrelated. The ductus arteriosus was narrowly patent. The pulmonary veins from the right and left lungs converged in the midline to form a common venous channel. The right aspect of this confluence had been sutured to the left atrium (Fig. 6), forming an opening between the left atrium and the pulmonary veins which admitted a 2 mm. probe. The anomalous common pulmonary venous channel extended downward to the esophageal hiatus anteriorly and to the right of the esophagus and penetrated the diaphragm to enter the abdomen; it terminated by joining a greatly enlarged portal vein (Fig. 7). No pulmonary or systemic veins

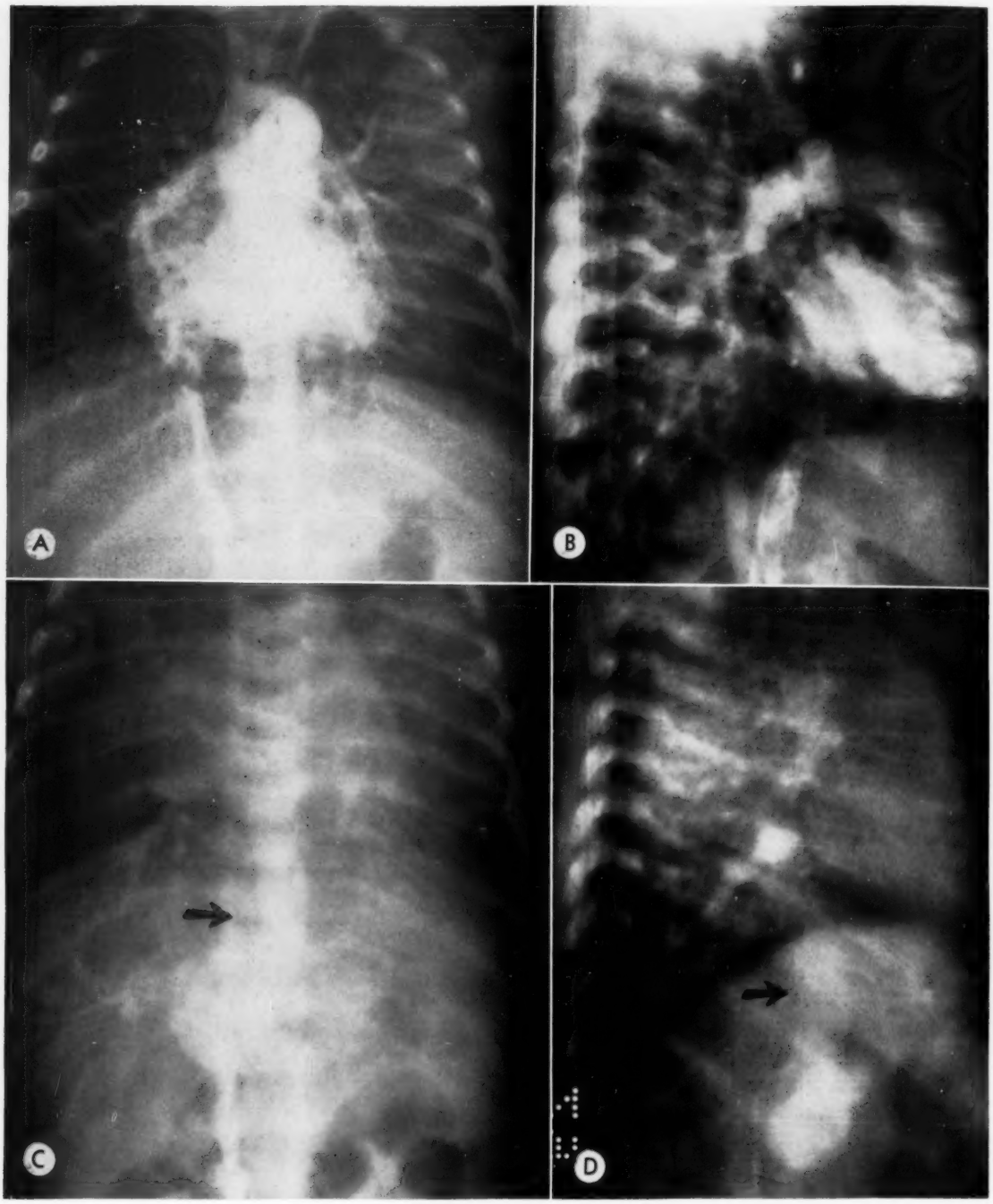

FIG. 5. Case II. Venous angiocardiograms. (*A*) Anteroposterior roentgenogram at 1 second shows the left atrium on each side of the midline, simultaneous opacification of equal density of a large pulmonary artery and a small aorta. (*B*) Lateral roentgenogram at 1 second shows the relative sizes of the pulmonary artery and aorta. (*C*) Anteroposterior roentgenogram at 5 seconds shows opaque material in the common pulmonary venous trunk, which terminates in the region of the porta hepatis. (*D*) Lateral roentgenogram at 5 seconds shows the common pulmonary vein (arrow) and its termination in the region of the porta hepatis.

entered the left atrium (except by way of the surgical anastomosis described). The ventricular septum was intact, and each valve was normal. A valvular competent patent foramen ovale was present. The lungs were observed to be congested.

The inadequate size of the surgical anastomosis between the left atrium and the pulmonary venous system may perhaps be explained by the smallness of the left atrium. It should be pointed out that the operation was performed with the circulation intact. Had artificial circulatory techniques been applied, the opportunity to create a larger opening might have been greater.

Case III.

Roentgenographic Findings. In a four week old white male infant a thoracic roentgenographic examination was performed in September 1960, during evaluation of cyanosis and dyspnea.

Fig. 6. Case II. Photograph of the gross specimen shows the surgically created anastomosis between the common pulmonary vein (C.P.V.) and the left atrium (L.A.). The probe is lying in the left atrium and is directed through the anastomosis into the common pulmonary vein. The diameter of the surgically created orifice was 2 mm. The right upper pulmonary vein (R.U.P.V.) and right lower pulmonary vein (R.L.P.V.) are seen at the upper left.

Fig. 7. Case II. Photograph of the specimen of the thoracic and abdominal organs viewed from behind, the esophagus having been removed. The common pulmonary vein (C.P.V.) formed by confluence of the individual pulmonary veins is of large caliber and enters a greatly enlarged portal vein (P.). The superior mesenteric vein (M.) and the splenic vein (above pancreas) are seen forming the portal vein. D.—diaphragm; L.—liver.

This study revealed the cardiac shadow to be of normal size and configuration. The lungs showed diffuse fine stippling bilaterally (Fig. 8). A diagnosis of pulmonary venous obstruction was made.

Venous angiocardiography was performed the following day. Six and one-half cubic centimeters of 90 per cent hypaque-M were injected into the right median basilic vein while films were exposed at two per second for fifteen seconds, in frontal and lateral projections. Following opacification of the right atrium, the left atrium filled, and simultaneous dense opacification of a large pulmonary artery and a small aorta then occurred (Fig. 9, *A* and *B*). Venous return of opacified blood from the lungs was delayed. At five seconds the pulmonary veins filled, and a large channel leading below the diaphragm to the portal vein opacified. (Fig. 10, *A* and *B*).

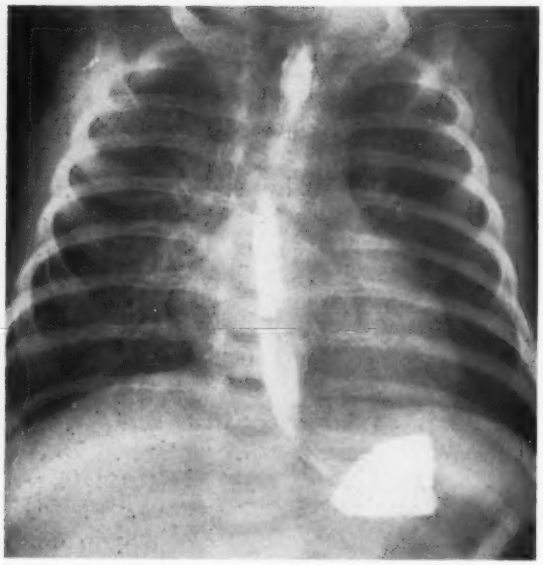

Fig. 8. Case III. Thoracic roentgenogram at 4 weeks shows normal cardiac size and reticular pulmonary markings.

On the sixth hospital day a thoracotomy was performed on the right side. Exploration revealed an anomalous pulmonary venous trunk receiving the venous tributaries from both lungs. This trunk was followed to its penetration of the diaphragm through the esophageal hiatus. When extracorporeal circulation was instituted, severe congestion and edema of the lungs developed. The extracorporeal circulatory procedure was discontinued, and with the circulation intact a side-to-side anastomosis of the anomalous pulmonary venous trunk with the left atrial wall was accomplished. No part of the anomalous pulmonary venous trunk was ligated or divided. Although the patient appeared to tolerate this procedure reasonably well, his condition gradually deteriorated and he died five hours after the operation.

Pathologic Findings. Abnormalities were restricted to the cardiovascular system. The great vessels were normally interrelated. A patent ductus arteriosus having a diameter of 1.4 cm. was noted. The four pulmonary veins joined in the midline to form a common channel that descended anteriorly and a little to the right of the esophagus and penetrated the diaphragm through the esophageal hiatus. This vessel then joined the portal vein (Fig. 10*C*). The surgically performed anastomosis between the left atrium and the common pulmonary venous trunk was identified. The suture line was intact, and the opening measured 4 mm. in diameter (Fig. 11). The ventricular septum was intact. A patent foramen ovale was adjudged to have a potential diameter of 6 mm. The common pulmonary venous trunk was patent throughout, measuring 8 mm. at its narrowest diameter.

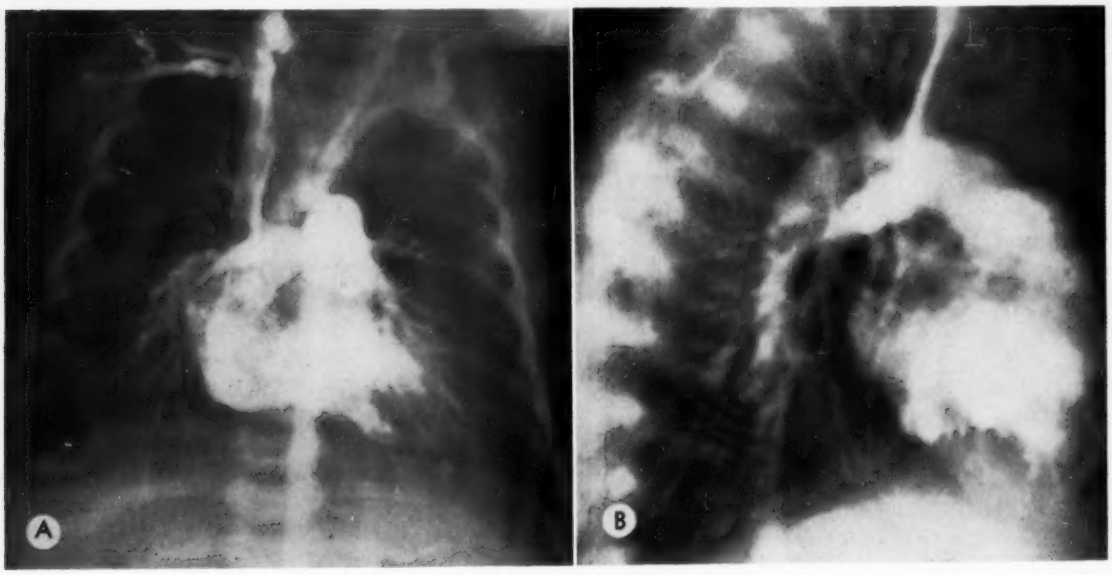

Fig. 9. Case III. Venous angiocardiograms at 1.5 seconds. (*A*) Anteroposterior roentgenogram shows a right-to-left shunt at the atrial level and simultaneous opacification with equal density in the large pulmonary artery and the small aorta. (*B*) Lateral roentgenogram shows opaque material in the left atrium and the enlargement of the pulmonary artery. The descending aorta is clearly evident.

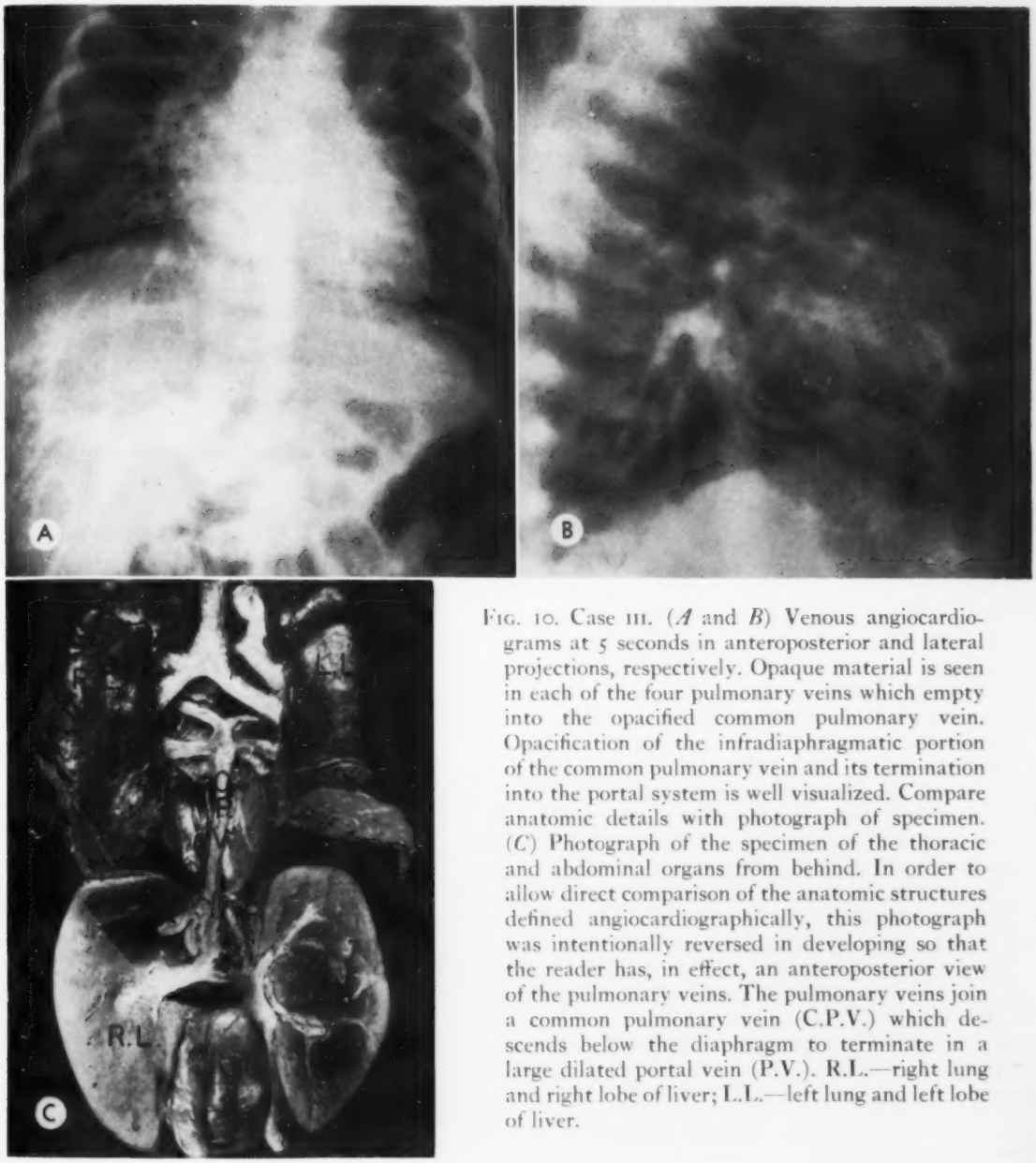

Fig. 10. Case III. (*A* and *B*) Venous angiocardiograms at 5 seconds in anteroposterior and lateral projections, respectively. Opaque material is seen in each of the four pulmonary veins which empty into the opacified common pulmonary vein. Opacification of the infradiaphragmatic portion of the common pulmonary vein and its termination into the portal system is well visualized. Compare anatomic details with photograph of specimen. (*C*) Photograph of the specimen of the thoracic and abdominal organs from behind. In order to allow direct comparison of the anatomic structures defined angiocardiographically, this photograph was intentionally reversed in developing so that the reader has, in effect, an anteroposterior view of the pulmonary veins. The pulmonary veins join a common pulmonary vein (C.P.V.) which descends below the diaphragm to terminate in a large dilated portal vein (P.V.). R.L.—right lung and right lobe of liver; L.L.—left lung and left lobe of liver.

The presence of a large patent ductus arteriosus undoubtedly accounted for the severe congestion of the lungs that developed when extracorporeal circulation was established. This pulmonary insult obviously did not enhance the child's chances for survival.

Case IV.

Roentgenographic Findings. A thirteen day old white male infant had a thoracic roentgenogram taken in November 1960, during evaluation of cyanosis and dyspnea. Cardiac size and contour were normal and diffuse reticular markings were observed in both pulmonary fields (Fig. 12*A*). Pulmonary venous obstruction was diagnosed, and venous angiocardiography was performed immediately. Six cubic centimeters of 90 per cent hypaque-M were injected into the right saphenous vein while films were exposed in frontal and lateral projections at two per second for fifteen seconds. Opacification of the right atrium was followed immediately by fill-

ing of the left atrium (Fig. 12*B*). Simultaneous dense opacification of a large pulmonary artery and a small aorta then occurred (Fig. 12*C*). Pulmonary veins were visualized at four and one-half seconds (Fig. 12*D*). No reopacification of the left atrium occurred, but, at ten and one-half seconds in the frontal projection, a globular collection of opaque material was seen to the left of the midline between the fifth and sixth ribs (Fig. 12*E*). On the lateral projection (Fig. 12*F*), this shadow lay immediately behind the heart. A faintly opacified channel between the globular shadow and the diaphragm was also seen on the lateral roentgenogram. A diagnosis of anomalous pulmonary venous connection with obstruction was made. The patient died several hours after this procedure and before surgical treatment could be instituted.

Pathologic Findings. Abnormalities were confined to the cardiovascular system. The heart appeared normal to external examination. The pulmonary artery and aorta were normally interrelated, and the ductus arteriosus was closed. No vessels entered the left atrium. The right pulmonary veins entered separately into a muscular walled chamber measuring 1 × 1.5 cm. and having the internal and external appearance of an accessory atrial chamber. Histologically, cardiac muscle was present in the wall of this chamber, which was connected by an atretic strand to the left atrium (Fig. 13, *A* and *B*). The accessory chamber and the two left pulmonary veins converged to form a common venous channel that descended in the midline, pierced the diaphragm through the esophageal hiatus, and terminated in the ductus venosus.

While the common pulmonary venous trunk itself was not narrowed, the upper part of the ductus venosus measured only 1 mm. in diameter. Below the level of entrance of the anomalous pulmonary vein, the ductus venosus was closed; therefore, the only open avenue for escape of pulmonary venous blood was by way of the narrowly patent segment of the ductus venosus into the left hepatic vein. We believe that the accessory atrium-like venous chamber opacified during angiocardiography and presented as a retrocardiac shadow as demonstrated in Figure 12, *E* and *F*.

HISTOLOGY OF THE LUNGS

The lungs were similar histologically in all patients (Fig. 14, *A–D*). Pronounced

Fig. 11. Case III. Photograph of specimen shows the surgically created anastomosis between the common pulmonary vein (C.P.V.) and the left atrium (L.A.). The probe lies in the left atrium and enters the common pulmonary vein through the anastomosis which measures 4 mm. in diameter. R.P.—right upper and lower pulmonary veins; L.P.—left upper and lower pulmonary veins; A.—aortic arch.

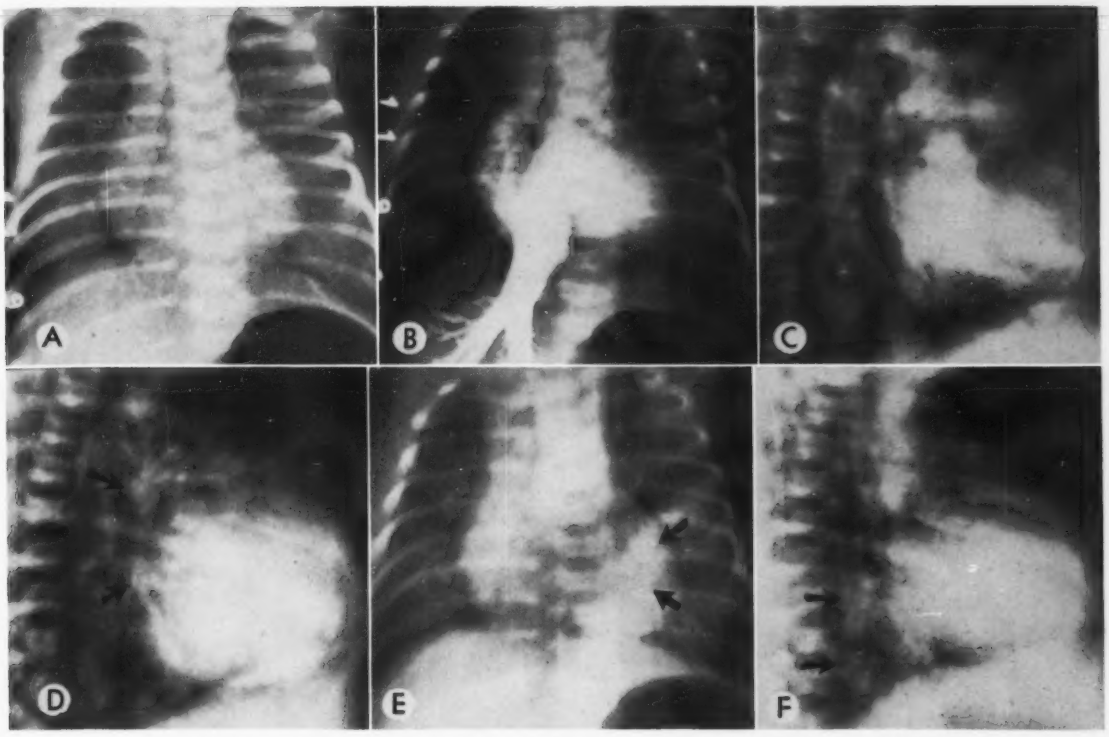

Fig. 12. Case IV. (*A*) Thoracic roentgenogram taken when patient was 13 days of age shows normal cardiac size and reticular pulmonary markings. (*B*) Venous angiocardiogram at 1 second shows right-to-left shunt at atrial level. (*C*) Venous angiocardiogram at 3 seconds shows simultaneous and equal opacification of a large pulmonary trunk and a small aorta. (*D*) Lateral venous angiocardiogram at 4½ seconds shows opacification of pulmonary veins (arrows). (*E*) Venous anteroposterior angiocardiogram at 10½ seconds shows a globular collection of opaque material in relation to the cardiac shadow (arrows). (*F*) Lateral venous angiocardiogram at 10½ seconds shows the globular shadow seen in *E* as lying immediately behind the left atrium. The arrows demonstrate an opacified channel descending toward the diaphragm.

thickening of the alveolar walls resulted from massive capillary dilatation. Hemosiderosis was present, and lymphatic channels in the visceral pleura and interlobular septa were dilated. The pulmonary arterioles revealed pronounced medial hypertrophy in excess of that normally found in this age group. The walls of the pulmonary veins were thickened as a result of very pronounced medial hypertrophy.

DISCUSSION

Total pulmonary venous connection with a vein below the diaphragm is but one of the anomalies possible when no direct communication exists between the left atrium and the pulmonary veins. The more common anomalous connections are between pulmonary veins on one hand, and the left innominate vein, the superior vena cava, coronary sinus, or right atrium on the other. Under these circumstances obstruction to pulmonary venous flow is rare. The clinical and roentgenographic signs in these patients are usually secondary to increased pulmonary blood flow and volume overload of the right ventricle.

When the pulmonary venous blood returns to the right atrium anomalously by way of the portal system of veins, among the factors which combine to increase the resistance to this flow are: (1) the narrow caliber of the common venous trunk and (2) the length of the anomalous route. Interposition of the hepatic capillary bed as in Cases I, II and III or the narrowness of the ductus venosus as in Case IV are additionally contributing factors.

The diagnosis of pulmonary venous obstruction may be suspected from clinical

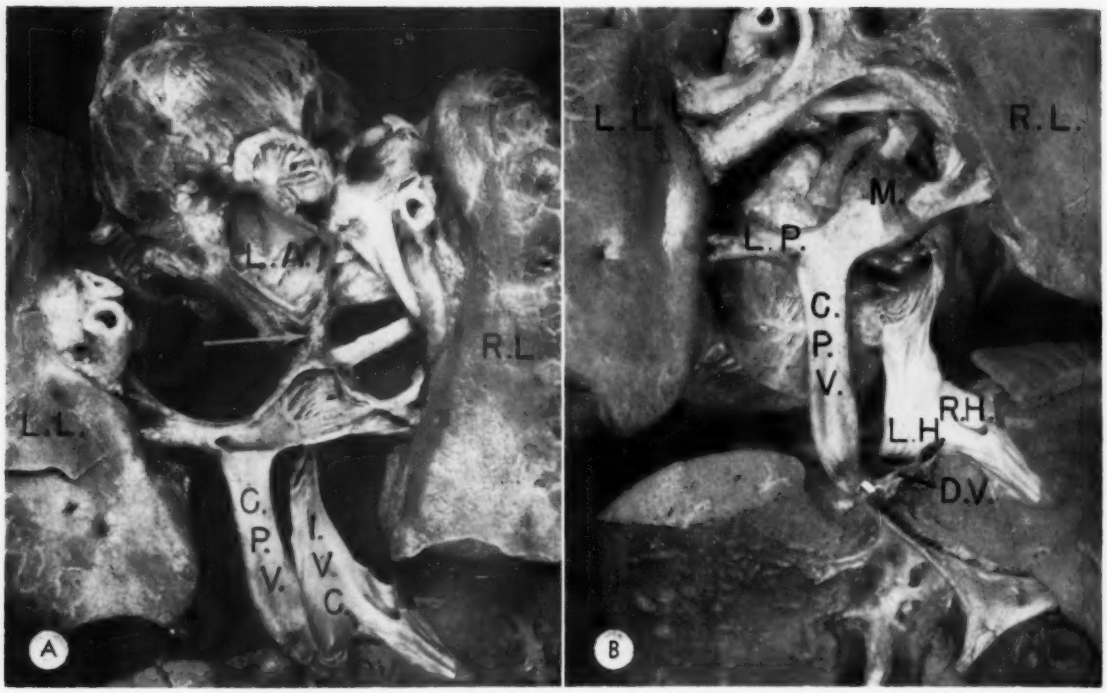

Fig. 13. Case IV. (*A*) Photograph of specimen of the thoracic and abdominal organs viewed from behind. The pulmonary artery and bronchus of the left lung (L.L.) have been severed. The apex of the heart has been elevated. The pulmonary veins from the right lung (R.L.) enter separately into a dilated thick-walled chamber that has the gross texture of an atrial chamber. The only outlet for this chamber is through a common pulmonary vein (C.P.V.) which also receives the veins of the left lung. The anomalous atrial-like chamber was connected to the left atrium (L.A.) by an atretic strand (arrow). The common pulmonary vein terminates below the diaphragm in the ductus venosus (D.V.). The ductus venosus is narrow and terminates in the left hepatic vein. The two hepatic veins join the inferior vena cava (I.V.C.) through which the pulmonary venous blood is finally delivered to the right atrium. (*B*) Photograph of the thoracic organs and liver viewed from behind. The essentials are like those illustrated in (*A*). This view emphasizes the presence of an atrial-like chamber (M.) formed by confluence of the veins from the right lung (R.L.). Histologically, the wall of this chamber was formed mostly of cardiac muscle. L.L.—left lung; L.P.—left pulmonary vein; D.V.—ductus venosus; L.H.—left hepatic vein; R.H.—right hepatic vein.

findings. Thus, any infant in the first few days or weeks of life presenting with cyanosis and dyspnea should be given immediate roentgenographic examination.

Among the findings on the thoracic roentgenogram, a cardiac shadow of normal size with peculiar pulmonary vascular markings should strongly suggest pulmonary venous obstruction. At this point, the differential diagnosis includes the types of pulmonary parenchymal disease occurring not infrequently in the neonatal period. Likewise, pulmonary venous obstruction results from a number of anatomic conditions. These include: (1) cor triatriatum,[15] (2) stenosis or atresia of the pulmonary veins,[12] (3) mitral atresia,[3] and (4) anomalous pulmonary venous connection to other systemic veins through stenotic channels, as well as (5) total anomalous pulmonary venous connection to the portal venous system.

The diagnosis of total anomalous pulmonary venous connection to *any* site, whether or not obstruction to pulmonary venous flow exists, may be made on the basis of the following four signs,[7] each of which was present in every one of our cases: (1) immediate shunt from right atrium to a normal sized or small left atrium; (2) no dilution of the contrast material in the left atrium; (3) simultaneous

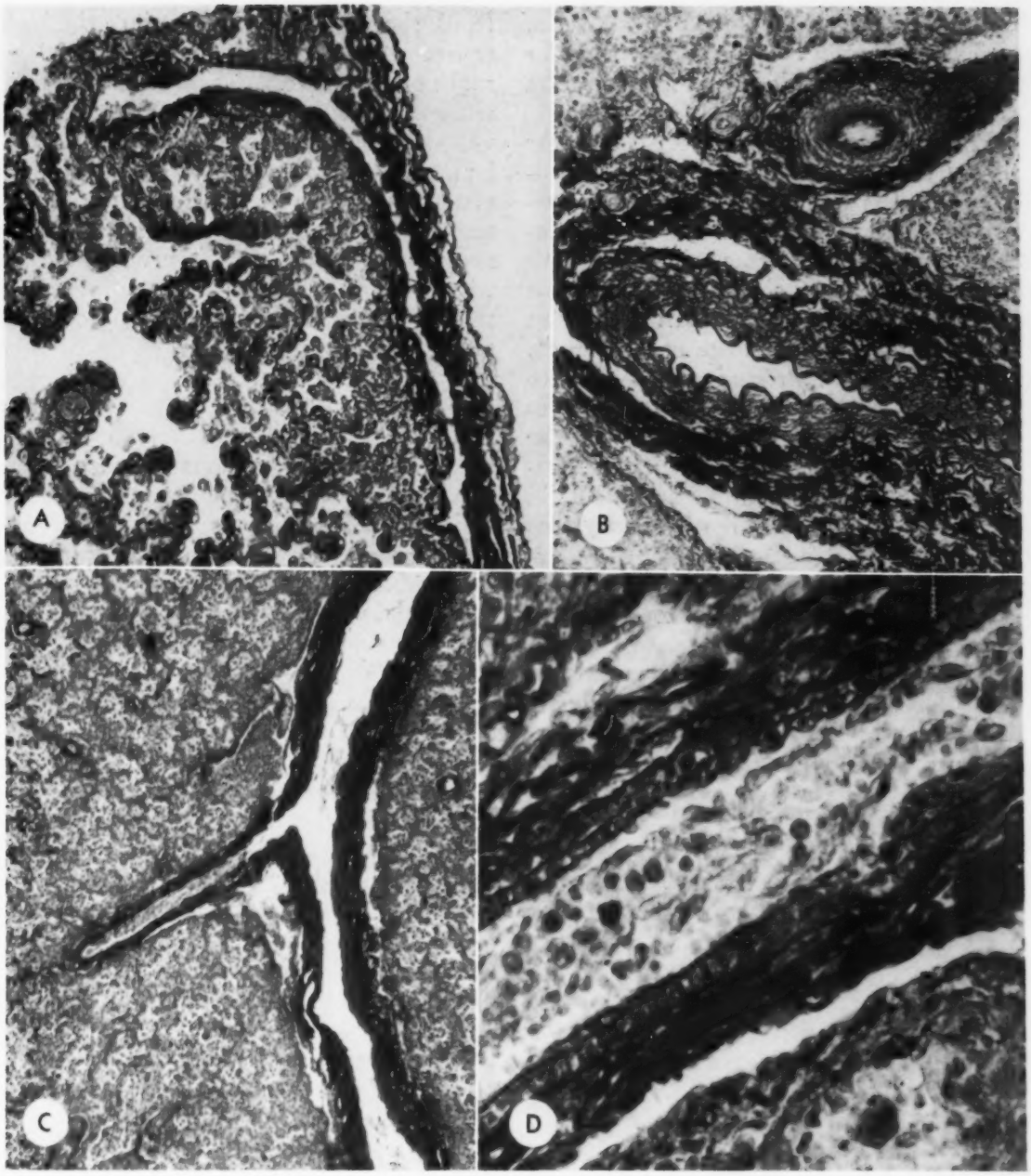

Fig. 14. Photomicrographs of pulmonary vessels from sections stained for elastic tissue. (*A*) Case I. Peripheral portion of lung and visceral pleura show dilatation of a pleural lymphatic and of the pulmonary capillaries (×170). (*B*) Case I. Medial hypertrophy of a large muscular artery and of an arteriole (upper portion of illustration) and an elastic artery are present (×135). (*C*) Case III. A venous trunk receives a tributary. Each shows a thick wall (×150). (*D*) Higher magnification of tributary shown in *C*. The prominence of muscle in the medial layer resembles that seen in arteries. Adventitial prominence is also present(×380).

opacification of an enlarged pulmonary artery and a small aorta; and (4) density of opacification of the aorta equal to or greater than that of the pulmonary artery.

The diagnosis of obstruction in the anomalous venous pathway depends on the foregoing characteristics and, in addition, the signs of: (a) delay in emptying of the

right side of the heart, (b) persistence of opacified blood in the pulmonary vascular system, and (c) failure of reopacification of the left atrium.

Precise anatomic demonstration of the site of anomalous connection of the pulmonary veins with the portal venous system may be established through angiocardiography. The characteristic finding is opacification of the anomalous venous channel with accumulation of contrast medium in the region of the porta hepatis. Low cardiac output and obstruction to pulmonary venous flow may combine to cause late or scant opacification of the anomalous pulmonary venous trunk. Therefore, the angiocardiographic study should be programmed to include roentgenograms taken ten to twelve seconds after the injection is made.

In Case IV, the diagnosis of total anomalous venous connection with obstruction was made on the basis of the presence of each of the aforementioned features. The significance of the opacification shown in Figure 12, *E* and *F* was not fully appreciated until pathologic confirmation.

A helpful clinical sign in each of our 4 cases was intensification of dyspnea and cyanosis during feeding. If one recalls that the anomalous common pulmonary venous trunk accompanies the esophagus through the same hiatus of the diaphragm, this clinical feature may be explained.

In total anomalous connection of the pulmonary veins to the portal venous system, the universal mortality of patients in the first few months of life dictates a prompt attempt to establish a definitive diagnosis. Following diagnosis, immediate surgical correction of the anomaly should be planned. On the basis of our experience to date, we believe that a cardiopulmonary bypass procedure should be utilized to allow the surgeon ample opportunity to make an adequate and accurately placed anastomosis. It is imperative that a patent ductus arteriosus, if present, be ligated prior to the institution of bypass. We feel that the anomalous pulmonary venous trunk should be left patent, since the high resistance imposed by this anomalous route of flow favors drainage through the anastomotic site but at the same time provides a safety valve should the left atrium be unable to accept the whole pulmonary venous return immediately. This pulmonary venous trunk could be ligated later if necessary. Only experience will indicate whether such a channel left open will close spontaneously if the anastomotic connections are adequate.

SUMMARY

1. The universal early mortality in patients with total anomalous venous connection to the portal venous system without major associated cardiac lesions necessitates prompt diagnostic and therapeutic measures.

2. The anatomic features present in this form of anomalous pulmonary venous connection are responsible for pulmonary venous obstruction.

3. On the basis of the clinical, physical, electrocardiographic, and routine roentgenographic findings, a diagnosis of pulmonary venous obstruction may be made in these patients.

4. Angiocardiography provides confirmation of the pulmonary venous obstruction and allows a definitive anatomic diagnosis of total anomalous pulmonary venous connection to the portal venous system.

5. Attempts to correct this condition surgically in 2 of 4 patients met with failure, but on the basis of this experience, it is believed that surgical correction of this defect remains feasible.

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CONGENITAL PULMONARY LYMPHANGIECTASIS*

REPORT OF A CASE WITH ROENTGEN FINDINGS

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CONGENITAL pulmonary lymphangiectasis, although relatively rare, has been fairly frequently the subject of papers appearing in the pathologic literature. It has been variously termed "congenital lymphangiomatosis of the lung,"[2] "congenital pulmonary cystic lymphangiectasis,"[1,3] and "congenital dilatation of pulmonary lymphatics."[5] Twenty-one cases have been reported in the world literature according to Frank and Piper[1] in their article published in 1959; however, we have been unable to find any description of this condition in the radiologic literature.

The cases previously described, as well as the present case, appear to have a fairly uniform clinical picture: that of neonatal respiratory distress and cyanosis with death occurring in a few hours or a few days. Some cases have also been observed in stillborns. Most often, the delivery and gestation have been uneventful.

Of the cases reported, we have been able to find only 2 of which roentgenograms were made. These, in addition to the present case, apparently represent the only cases of congenital pulmonary lymphangiectasis which have been brought to the attention of the radiologist. Because of the clinical similarity of this disease to other conditions more familiar to the radiologist, we feel that our patient in whom the roentgenographic findings could not be distinguished from those of hyaline membrane disease or fetal atelectasis is worthy of reporting. Maidman and Barnett[5] have stated, "It is apparent from a review of all cases that this entity . . . must be included with other disease processes responsible for neonatal cyanosis and, unfortunately, can be positively identified only by means of autopsy."

The roentgenograms of the 2 previously reported cases appear to be similar to those of the present case, although the changes are probably more marked. The findings were described as "bilateral multiple scattered densities,"[5] and "an enlarged heart and increased opacity of both lung fields with some mottling suggestive of diffuse cystic change." In the latter case, the heart appeared "somewhat dilated" at necropsy, so definite cardiomegaly may not have been present.[4]

REPORT OF A CASE

On November 1, 1960, at 10:45 P.M., the patient was born at full term by low forceps delivery. He weighed 7 pounds and 6 ounces. At birth, the heart rate was rapid, respirations were rapid and shallow, and the infant was cyanotic. The liver was thought to be enlarged. The infant was placed in a rocking-bed respirator and given moist oxygen.

A portable anteroposterior chest roentgenogram made approximately twelve hours following birth showed a normal heart, widening of the anterior and superior mediastinal regions, indicating a thymus gland, fine granular densities distributed throughout both lungs and a normal position of the diaphragm. The bony thorax showed no abnormality. The diffuse granular pulmonary densities, coupled with the clinical history, were thought to represent hyaline membrane disease (Fig. 1, *A* and *B*).

About fourteen hours after birth, the infant was digitalized and a liquefying agent (Chymar aqueous) was given. Penicillin therapy was also started. The infant failed to respond and expired approximately sixteen hours after birth.

At autopsy, the liver was found to be grossly enlarged, extending into the left side of the abdomen. The sinusoids were dilated and filled

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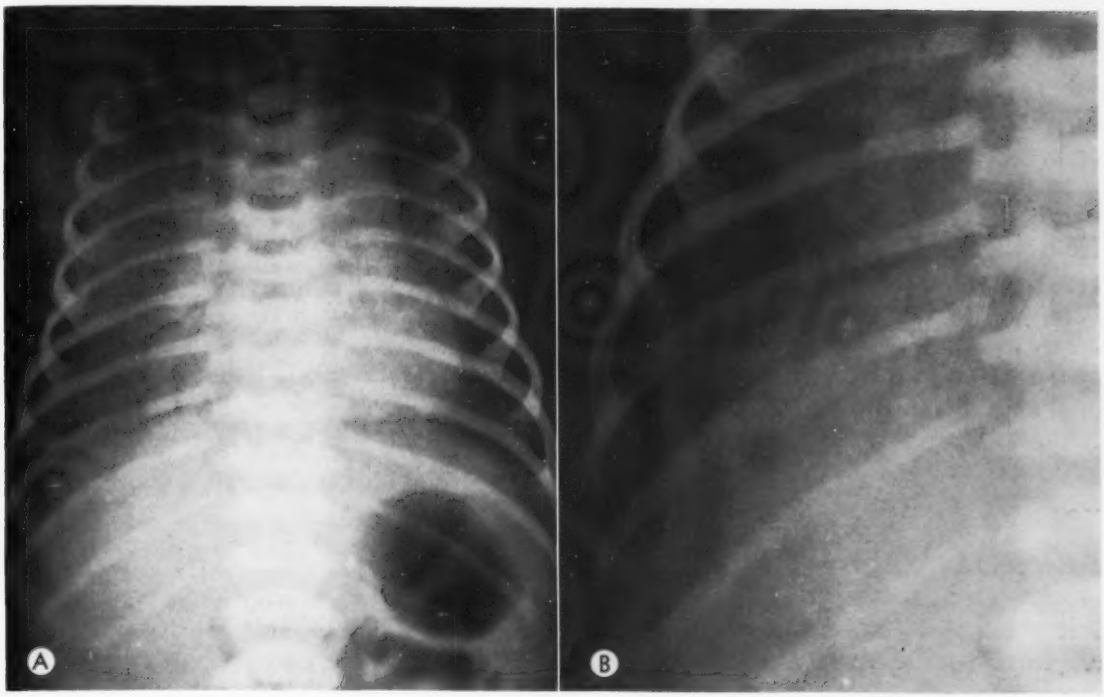

Fig. 1. (*A*) Fine granular densities are distributed throughout both lungs, representing markedly dilated cystic lymphatics. This picture cannot be distinguished from that in hyaline membrane disease or in fetal atelectasis. (*B*) Detail of the right lower lung field shows the diffuse granular densities.

with blood. Scattered throughout the liver were numerous small collections of immature blood cells. The thymus was of normal size and showed numerous areas of hemorrhage which were relatively small, although in some instances, the hemorrhage became confluent and covered a fairly large area. The heart was normal.

Both lungs were of normal size. The pleural surfaces were smooth and glistening. The surface and cut surface of both lungs were of a healthy pink color. Microscopic examination showed the alveolar spaces to be moderately enlarged. In the interstitial tissue and particularly just beneath the pleura, the lymphatics were markedly dilated. This picture was noted in all of the sections of lung studied microscopically. In some areas, the alveolar spaces contained a few squames; however, there was very little inflammatory reaction at any point in the lungs. No evidence of hyaline membrane disease was found (Fig. 2).

A physiologic patent ductus arteriosus and patent foramen ovale were noted. The cranial cavity was not entered.

The final anatomic diagnosis was (1) congenital pulmonary lymphangiectasis, (2) passive congestion of the liver, (3) petechiae of the thymus, (4) extramedullary hematopoiesis of the liver, (5) patent foramen ovale (physiologic), and (6) patent ductus arteriosus (physiologic.)

COMMENT

Congenital pulmonary lymphangiectasis is a condition occurring in newborns and to

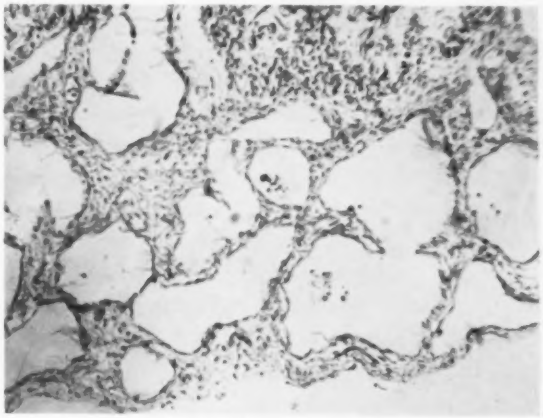

Fig. 2. Photomicrograph showing the dilated lymphatics in the lung.

a lesser extent in stillborns. In most instances gestation and delivery are normal but the child commences to have respiratory distress and cyanosis within minutes or a few hours after birth. Because of the increasing frequency with which roentgenography of the newborn in respiratory distress is performed, it is important that the radiologist be aware of this disease and its roentgen similarity to more familiar conditions. Although we have been unable to find a description of the roentgen findings in the radiologic literature, it is likely that this condition is much more common than previously realized, and that many cases formerly diagnosed as congenital heart disease, hyaline membrane disease, fetal atelectasis, etc., and which were not pathologically confirmed may have represented this condition. It is anticipated that this diagnosis will be made more frequently in the future.

SUMMARY

1. The first case of congenital pulmonary lymphangiectasis reported in the radiologic literature is presented.

2. The clinical symptoms of congenital pulmonary lymphangiectasis simulate hyaline membrane disease and some types of congenital heart disease.

3. The roentgenographic findings in congenital lymphangiectasis of fine granular densities distributed throughout the lungs simulate those of hyaline membrane disease and fetal atelectasis.

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Vol. 86, No. 3

ESOPHAGEAL STRICTURE FOLLOWING INGESTION OF CLINITEST TABLETS*

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ESOPHAGEAL strictures following the accidental ingestion of Clinitest tablets have recently been described in the pediatric and otolaryngologic literature. These commercially available tablets are used at home by patients with diabetes to test for glycosuria. The tablets contain anhydrous sodium hydroxide and therefore represent a new type of lye ingestion hazard. Since the Clinitest stricture has certain characteristic features, a report of such a case in the radiologic literature appears justifiable.

REPORT OF A CASE

A sixteen year old girl was admitted to the Kings County Hospital on July 13, 1959, one day after she inadvertently swallowed two Clinitest tablets, used by her father, a diabetic. She had mistaken them for aspirin. Immediately after swallowing the pills the patient felt a burning sensation substernally and regurgitated the partially dissolved tablets. Inasmuch as the burning sensation persisted the patient was admitted for observation. There were no abnormal physical findings. Esophagoscopic examination on July 15, 1959 revealed only minimal congestion of the esophagus. She was treated for her symptoms, improved clinically and left the hospital two days later. One week thereafter she began to have difficulty swallowing solid foods. She experienced a sensation of heaviness in the chest during and after meals. This was associated with occasional vomiting. She returned to the hospital and a roentgenologic examination of the esophagus on July 30, 1959, revealed a short, well circumscribed constriction at the junction of the middle and lower thirds of the esophagus (Fig. 1*A*). A small ulcer crater arose from the posterior aspect of the constricted area (Fig. 1*B*). The esophagus was not dilated proximal to the lesion and there was no delay in the descent of the thick barium mixture. Exophagoscopic examination revealed a short ring-like stricture approximately 33 cm. from the upper incisor teeth. Stretching with Hurst dilators was performed almost daily until a No. 28 dilator was passed. An esophagram obtained on August 10, 1959 showed some widening of the previously noted stricture and no ulceration was noted. The patient had no further difficulty in swallowing solid foods and was discharged from the hospital on August 13, 1959.

PATHOGENESIS

Caustic urine-sugar reagent tablets (Clinitest) contain sodium hydroxide, sodium bicarbonate, citric acid and copper sulfate. Sodium hydroxide liberates a large amount of heat on hydration when placed in solution and if this occurs in the esophagus a thermal burn of the mucosa results. The caustic action of sodium hydroxide causes direct necrosis. Copper sulfate is both astringent and irritant.[3,10,12]

Diffuse edema is the initial pathologic effect of lye ingestion. Occasionally, this may be demonstrated by an esophagram. However, roentgenologic studies performed during this phase in the previously reported cases of Clinitest tablet ingestion have revealed no changes of diagnostic or prognostic significance.[2,10] Liquefaction necrosis follows rapidly with sloughing of the necrotic material. Repair begins at about the end of the second week and the resulting fibrosis leads to stricture formation.

Since the accident under consideration in all likelihood involves the arrest of a firm tablet during its passage through the esophagus, it is quite understandable that the resultant stricture is short and ring-

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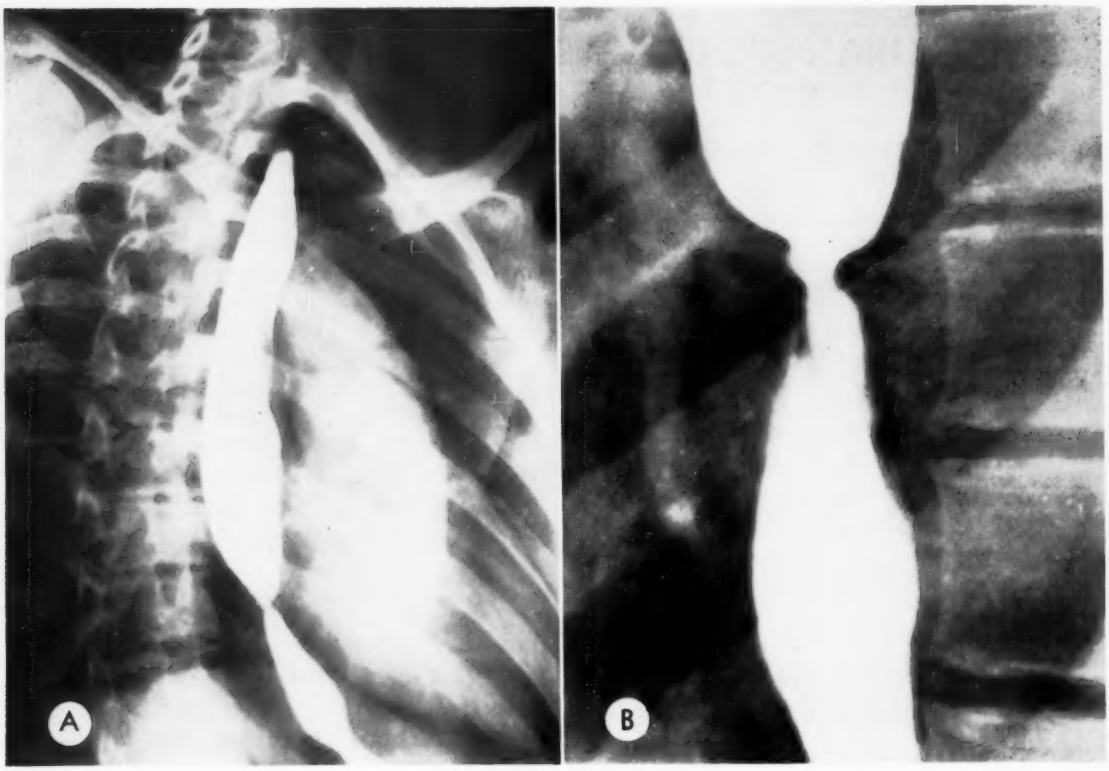

FIG. 1. (*A*) Roentgenogram demonstrates the short, ring-like stenosis of the esophagus at approximately the junction of the middle and lower thirds. The esophagus proximal and distal to this area is normal. (*B*) Spot roentgenogram of the strictured area shows the small ulcer crater arising from the posterior portion of the esophageal wall.

like. This differs from the usual type of lye ingestion—drinking a caustic solution—in which the stricture is usually elongated and has tapered ends. Arrest of the tablet can apparently occur at any of the usual areas of anatomic or physiologic narrowing particularly if only small amounts of water are ingested with the tablet. The previous case reports in the literature describe the occurrence of strictures in all portions of the esophagus. No changes need be produced if there is sufficiently rapid passage of the tablet through the esophagus or if an adequate amount of fluid is ingested simultaneously. One patient has been reported to have taken one tablet four times a day for several weeks. However, each tablet was swallowed with a full glass of water and no esophageal or gastric disorders were noted on follow-up examinations.[10] The stomach usually remains uninjured because of the neutralizing effect of the acid gastric secretions and the protective effect of gastric mucin.

ROENTGEN FINDINGS

The diagnosis of caustic tablet (e.g., Clinitest) stricture should be thought of when there is a smooth-walled, sharply-circumscribed, short ring-like constriction of the esophagus in an otherwise normal esophagus (Fig. 1, *A* and *B*). Because ulcer formation within the stricture is quite common, the lesion must be distinguished from peptic esophagitis. The latter is most frequently seen in the lower third of the esophagus and is often associated with an hiatus hernia. Ulceration arising in heterotopic gastric mucosa may produce the radiating mucosal folds so commonly found in gastric ulcers. The constricting annular "lower esophageal ring" should be easy to

distinguish because of its location at the gastroesophageal mucosal junction and its typical diaphragm-like appearance.[4] Diffuse systemic sclerosis with esophageal stricture formation has the characteristics of a chronic diffuse esophagitis. The presence of characteristic changes in peristalsis and in the emptying mechanism together with scleroderma involving the hands, feet or face should lead to the correct diagnosis. Epidermolysis bullosa produces an esophageal stricture which is usually smooth, somewhat lengthy and tapers at both ends. It is always accompanied by cutaneous manifestations.[1] Congenital esophageal webs are usually located on the anterior wall of the esophagus at the level of the cricoid cartilage. Conceivably, an infiltrative neoplasm could simulate a benign stricture but since most of the reported cases are in children the differential diagnosis of a neoplasm may arise in only the occasional case found in adults.

CLINICAL COURSE

Of the 7 cases thus far reported in the literature, 5 have been in children. The clinical course following the ingestion of Clinitest tablets is quite similar to that following ordinary lye ingestion. Early cortisone and antibiotic therapy has been recommended to prevent stricture formation.[8] Treatment in our case has been limited essentially to bougienage. Whether more dilatation will be required in the future cannot be determined at this time. Where persistent narrowing existed, simple resection with end to end anastomosis has been successful.[2,10,12]

SUMMARY

Caustic urine-sugar reagent tablets (Clinitest tablets) are widely used by the laity and cases of accidental ingestion continue to occur. The radiologist should be aware of the characteristic smooth-walled, sharply circumscribed, short ring-like stricture which may be produced.

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ANOMALOUS POSITION OF THE FOREGUT*

By BERTA M. RUBINSTEIN, M.D., HOWARD BLOOM, M.D., REGINA GLUCK, M.D., *and* MILTON J. H. GRAND, M.D.
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MANY excellent reviews on malrotation of the bowel have appeared in recent publications, but these have dealt for the greater part with abnormalities in the embryologic positioning of the midgut portion of the primitive gastrointestinal tract. Little has been said, regarding the anomalous position of the foregut and its anlage. The case presented is a two and one-half year old white girl with congenital heart disease. While undergoing routine roentgenologic examination for this condition, she was found to have an abnormally located stomach, which at first suggested situs inversus, but was later shown to be a case of failure of rotation of the foregut.

REPORT OF A CASE

This two and one-half year old female was first seen at Montefiore Hospital on March 16, 1959 for investigation of congenital heart disease. Her birth weight on March 3, 1956 was 7 pounds 15 ounces. Cyanosis was noted shortly after birth and vomiting occurred at the same time. Roentgen findings at that time indicated an "upside down stomach with partial obstruction." She was transferred to Meadowbrook Hospital at the age of one week, and repeat roentgenograms indicated "situs inversus abdominalis with no obstruction." The vomiting was controlled by careful feeding, and the gastrointestinal disturbances subsided. At the age of two weeks she went into acute cardiac failure which was controlled with digitalis. She was discharged at the age of one month, when she had regained her birth weight. The patient did well at home except for persistence of slight cyanosis. At the age of five months, following an episode of diarrhea, the cyanosis increased and she went into syncope during crying spells. She suffered no further episodes of cardiac embarrassment, but she developed slowly, and by the age of two years, she could not walk without support and weighed only 18 pounds 10 ounces. In June, 1958, at the age of twenty-six months, she developed a left hemiplegia and congestive heart failure. She was digitalized, and put on mercurials and salt restriction, but her condition did not clear up, and she was admitted to Montefiore Hospital for further investigation.

Physical examination revealed an underdeveloped girl who had resting cyanosis, clubbing of the fingers and toes and peripheral edema. Rales were heard in both lungs and fluid was present. The liver was palpated 6 cm. below the right costal margin. The blood pressure was 90/60, and the heart rate was regular at 120 per minute with a loud systolic murmur, heard best in the left fourth interspace at the sternal edge. A precordial bulge was evident and the heart was enlarged to percussion. On neurologic examination no residual of her earlier hemiplegia was found.

Laboratory Data. Hematocrit was 66 per cent, the hemoglobin was 20 gm. per cent, the red blood cell count was 7,230,000 per cu. mm., the white blood cell count was 8,900 per cu. mm. with 79 per cent polymorphonuclears, 20 per cent lymphocytes and 1 per cent monocytes. The platelet count was 170,000 per cu. mm. Specific gravity of the urine was 1.009 with a trace of albumin but without sugar or white cells. An electrocardiogram revealed right ventricular hypertrophy.

Roentgen Findings. Fluoroscopy showed a bizarre cardiac shadow consistent with transposition of the great vessels. Roentgenography with barium in the esophagus (Fig. 1 and 2) disclosed marked enlargement of the cardiac silhouette with the left border reaching almost to the left lateral chest wall. These studies and roentgenograms of the upper gastrointestinal tract showed the stomach to be located in the right side of the abdominal cavity with the greater curvature on the right and the lesser curvature on the left (Fig. 1 and 3). The pylorus

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and first part of the duodenum pointed across the midline to the left and anteriorly (Fig. 1, 2 and 4). The liver, however, was in the right upper quadrant (Fig. 3). On this basis, the diagnosis of failure of rotation of the foregut was made, rather than situs inversus abdominalis.

A selective angiocardiogram using 70 per cent Urokon outlined a large left ventricle, which gave rise to the aorta, situated to the left of the left pulmonary artery. The right and left pulmonary arteries were well visualized, but the main pulmonary artery could not be clearly delineated.

In view of the inability to establish a definitive diagnosis, a second injection was made into the left ventricle since the catheter could easily be passed through a large interatrial septal defect. During this second procedure, the child developed ventricular extrasystoles and then went into ventricular fibrillation with cardiac arrest. She did not respond to cardiac massage and died.

Necropsy Findings. At necropsy performed five hours after death, 100 cc. of clear yellow fluid was found in the peritoneal cavity. The position of the esophagus was unremarkable and it terminated in the cardia of the stomach at about 1 cm. beyond the diaphragmatic hiatus. The stomach lay within the right upper quadrant of the abdominal cavity with the cardia and greater curvature lying on the right while the lesser curvature was on the left. The pylorus pointed across the midline from the right side and the first part of the duodenum pointed anteriorly. The duodenum then continued to form a normal loop which was, however, concave to the right and terminated at the duodenojejunal junction which lay in the right upper quadrant. The jejunum and ileum were completely patent but were abnormally located, lying almost completely in the right lower quadrant of the abdominal cavity. The terminal ileum ascended in the midline up toward the diaphragm and entered the cecum

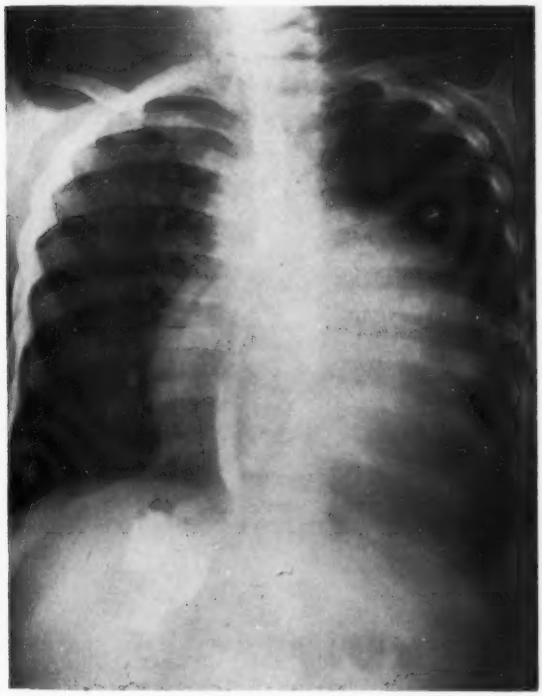

Fig. 1. Posteroanterior chest roentgenogram with the esophagus and upper stomach opacified with barium shows the heart markedly enlarged in its transverse diameter. The lower half of the esophagus is bowed to the right and the stomach is seen well to the right of the midline.

Fig. 2. A lateral roentgenogram of the chest with the esophagus, stomach and duodenal bulb opacified with barium shows the pylorus and duodenal cap pointed forward. Gas is seen in the postbulbar duodenal segment which is far anterior to its usual position.

FIG. 3. A frontal plane roentgenogram made during an upper gastrointestinal tract examination shows the barium-filled stomach to be well to the right of the midline. The greater curvature of the stomach is on the right side. The entire small bowel lies mostly on the right side of the abdomen. An opacity representing the liver is seen in the right upper quadrant.

at this point. The cecum, appendix and large bowel were unremarkable in appearance with no evidence of diverticula or stenosis, but were abnormally situated. The cecum lay in the upper part of the abdominal cavity near the midsagittal plane, while the colon ran from this point across the left half of the upper abdominal cavity to the splenic flexure, at which point it made a right angle turn and descended normally along the left side of the peritoneal cavity to the rectum, which descended in the midline of the pelvis to the anal orifice. In addition, the whole segment of colon was suspended from the posterior abdominal wall by a thin mesentery. The liver was normally situated in the right upper quadrant and appeared unremarkable. The head of the pancreas lay within the loop of the duodenum on the left side of the peritoneal cavity and extended across the midline to the right with the tail of the pancreas lying in the vicinity of the gallbladder. No spleen was noted within the peritoneal cavity and the normal peritoneal reflections could not be traced. The foramen of Winslow was also not identified. No other abnormalities were noted within the peritoneal cavity. In the thoracic cavity, no pericardial or pleural effusions were noted, but the lungs were grossly atelectatic and appeared to be compressed by a greatly enlarged heart which weighed 190 gm. The heart was a cor biloculare with a rudimentary right ventricle, an inter-atrial septum secundum defect, an interventricular atrioventricular communis defect, an infundibular pulmonic stenosis and total anomalous pulmonary venous drainage. The pulmonary artery and aorta both arose from

FIG. 4. A lateral roentgenogram made during an upper gastrointestinal tract examination confirms the impression obtained from Figure 2 where the pylorus and the duodenum are seen directed anteriorly.

the common left ventricle with the pulmonary valve ring lying to the right of the aortic valve ring. The peripheral distribution of the vessels from the pulmonary artery and aorta was unremarkable and the ductus arteriosus was not patent. This case, therefore, demonstrates multiple congenital anomalies involving the heart and gastrointestinal tract, as well as asplenia.

DISCUSSION

The primitive gastrointestinal tract develops as a straight tube suspended in the sagittal plane by a common dorsal mesentery. It may be divided into the foregut, *i.e.*, from the mouth to the duodenojejunal junction; the midgut, *i.e.*, from the duodenojejunal junction to the midtransverse colon; and the hindgut, *i.e.*, from the midtransverse colon to the anus.

FIRST STAGE OF MIDGUT ROTATION

As the primitive intestinal tract elongates, it bulges through the umbilical orifice into the primitive umbilical cord as a temporary physiologic umbilical herniation. Failure of rotation beyond the first stage and retention of the midgut loop in the umbilical stalk at birth results in a condition known as omphalocele.

SECOND STAGE OF MIDGUT ROTATION

Nonrotation. The midgut loop is returned to the peritoneal cavity from the temporary umbilical herniation without having rotated beyond the horizontal plane it occupied at the end of the first stage.

The small bowel is entirely in the right side of the abdomen, the colon in the left. The terminal ileum crosses the midline to enter the cecum from the right. The duodenum descends entirely on the right side of the vertebral column. Internal hernias are explained as anomalies of intestinal rotation.

Paraduodenal Hernia. This is represented by imprisonment of the small bowel under the mesentery of the right colon during the process of fixation of the midgut loop after its rotation.

Reversed Rotation. Clockwise instead of counterclockwise rotation of 180° occurs during this stage. The transverse colon lies under the superior mesenteric artery and the duodenum above it.

THIRD STAGE OF MIDGUT ROTATION

This entity is characterized by descent of the cecum from the subhepatic position into the right lower quadrant and fixation of the mesentery of the cecum and ascending colon in the right flank.

An anomaly of the third stage is the subhepatic cecum. The cecum fails to elongate and descend into the right iliac fossa. If, with the cecum in this position, there is also failure of fixation of the small bowel mesentery on a broad attachment to the posterior abdominal wall, volvulus of the entire small intestine may occur. Other anomalies include retrocecal appendix and mobile cecum which we will not discuss here.

COMMENT

Omphalocele as the prime anomaly of the first stage of midgut rotation, errors of the second stage of midgut rotation giving rise to torsion of bowel segments on an abnormally persistent mesentery with bowel obstruction, and internal hernias have been adequately described in the literature. However, cases of the most primitive position of the upper gastrointestinal tract with failure of fetal rotation of the stomach before the first stage of midgut rotation (prior to descent of the gastrointestinal tube into the umbilical cord) have rarely been reported.

Caffey, in his book of Pediatric X-ray Diagnosis describes congenital microgastria and lack of fetal rotation of the stomach with failure of the greater and lesser curvature to develop. There is no differentiation into the fundus, body, antrum and pyloric canal. The tiny tubular stomach remains in the midsagittal plane and is joined from above and behind at its summit by the esophagus. The duodenum projects directly ventrad from the pyloric end of the stomach. Vomiting from birth,

hematemesis, loss of weight, and secondary anemia are the chief clinical findings.

Our case is an example of the most primitive stomach lying in the right upper quadrant in the midsagittal plane with the pylorus and duodenal bulb directed ventrad. Failure of rotation of the foregut, in addition to anomalies of second stage midgut rotation, multiple congenital cardiac anomalies and asplenia were noted.

The combination of an absent spleen and congenital heart disease, also found by other investigators,[1,8,10] is apparently more than coincidental.

SUMMARY AND CONCLUSION

A case of anomalous position of the foregut and multiple congenital heart abnormalities as well as asplenia in a two and one-half year old female is presented in which the foregut anomaly was visualized by barium opacification. The roentgen findings were confirmed on autopsy.

The position of the stomach and duodenum in this case reflects the most primitive position of the foregut. The stages of midgut rotation and other gut anomalies are briefy described.

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Vol. 86, No. 3

HYPERTROPHIC HEMANGIOENDOTHELIOMA OF INFANCY*

SUCCESSFUL MANAGEMENT OF A CASE WITH THE PATHOLOGIC AND ROENTGEN THERAPY CRITERIA

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THE purpose of this report is to describe the successful management of a hemangioendothelioma of muscle in a newborn infant. A review of the pertinent literature is made and certain basic principles are stressed. The textbooks on radiotherapy give little information on this entity. The pathologic diagnosis can often lead to confusion, and the surgeon must be alerted to avoid extensive mutilating procedures. It is hoped that proper direction can be given from the experience gained in this study.

The difficulties that can arise in the pathologic diagnosis, in the surgical approach, and in the necessity for prolonged fractionation of radiation dosage are well illustrated in the following case report. The mother's refusal of surgical procedures, early and again later in the course, is probably the most significant factor in the results obtained.

REPORT OF A CASE

This four day old white female was admitted to the University of Illinois Hospitals on August 10, 1956. She was born at full term, delivery was spontaneous and she weighed 7 pounds. At birth, a large tumor on the left side of the upper back and scapula extending over the left clavicle and into the left side of the neck was noted (Fig. 1, *A* and *B*). The mass felt both hard and cystic in different areas. There appeared to be a light bluish tinge to the skin but the skin itself was not involved (Fig. 2). White blood cell count was 15,000, neutrophiles 83 per cent, lymphocytes 12 per cent, and monocytes 5 per cent, with adequate platelets.

The parents were opposed to any mutilating procedure of amputation of the arm. However, they did consent to a biopsy. On August 13, 1956, under general anesthesia the patient was explored. An incision was made over the mass posteriorly for at least 10 cm. The tumor mass lay beneath the latissimus dorsi, rhomboid and trapezius muscles. Biopsy of the mass was taken at the medial border, which was adjacent to the spinous processes and transverse processes of the vertebral bodies. There was no paraspinous musculature in this area. Since the parents had denied permission for removal of the entire upper extremity and the surgeon felt that local excision could not be accomplished, only a biopsy was done.

A frozen section was reported as a highly cellular sarcoma. Subsequent study of the tissue revealed sheets of tumor cells with small oval nuclei arranged in an irregular closely interwoven pattern. In some areas the cells had larger, pale staining nuclei and indistinct cytoplasm. In other areas the cells were spindle shaped and there were numerous small vascular spaces of capillary size, some containing red blood cells. The final impression was "malignant tumor of the shoulder region, with hemangioendotheliomatous qualities" (Fig. 3).

From August 23, 1956, to September 28, 1956, the patient received the first course of irradiation via multiple small 4×5 cm. oblique portals (anterior and posterior superior and inferior, and posterior medial and lateral) from a 220 kv. machine, 1.12 mm. Cu half value layer, 50 cm. distance, with a daily dose of 75 r to a portal. Each of five portals received approximately 700 r air dose.

In the early spring of 1957, the mother reported that there was some decrease in the size of the tumor (Fig. 4). A second course of irradiation was given June 19, 1957, to July 17, 1957, through eight small 4×5 cm. oblique tangential portals. The same quality of radiation was used as in the first course and each of the portals received a total air dose of 650 r. In the ensuing six months the surgeons felt that

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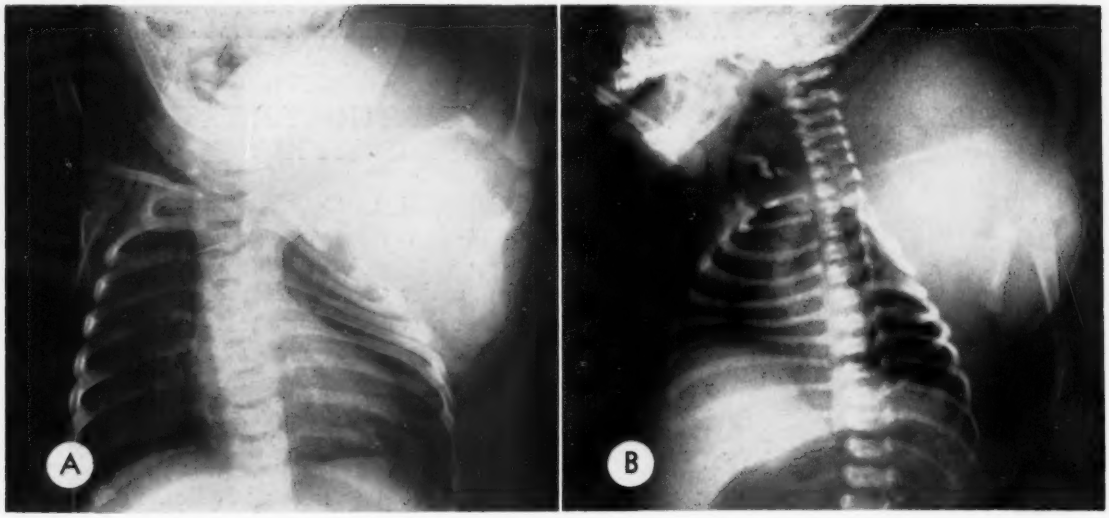

FIG. 1. (*A*) Anteroposterior and (*B*) left anterior oblique roentgenograms of the chest when the patient was nine days old. Note the large soft tissue tumor and the extent of deformity of the left upper thoracic rib cage. There is separation of the transverse processes of the lower cervical and upper thoracic vertebrae.

the lesion was now resectable, but the mother refused any surgical intervention.

In 1958, there was further slow steady reduction in the size of the mass. By this time there was no deformity of the thoracic rib cage (Fig. 5). The patient, when seen in January, 1961, revealed only the scar from the previous biopsy and a slight defect from the lack of development of normal musculature along the left superior paraspinal region, the site of previous tumor (Fig. 6).

DISCUSSION

Dargeon[1] cites a good clinicopathologic classification of lesions of vascular origin. Of the twelve categories, only two are of concern in this presentation: (a) hypertrophic hemangioma, and (b) hemangioendothelioma. His illustration of 2 cases of the hypertrophic form are exceedingly pertinent. One of them is a diffuse subcutaneous lesion of the skin itself. This grossly resembles the case being presented. However, all of his tabulated hypertrophic cases have associated thrombocytopenic purpura. Dargeon also stated that in the therapy of this lesion, roentgen therapy is frequently unsatisfactory and surgery may be required. Southard *et al.*[3] reported a twenty-one day old infant who had a capillary hemangioma of the left leg and purpura. The lesion received 3,360 r in twenty days, and three weeks later had completely disappeared. Three months later, a second course of 2,400 r was given for an extension. Contracture and radiation fibrosis was reported.

FIG. 2. Clinical appearance before irradiation, when the patient was seventeen days old. Note the lack of any skin involvement.

Watson and McCarthy[6] have written on a hypertrophic or angioblastic type of hemangioma. They stated that this appears chiefly in the skin as a solid elevated purplish red lesion. They further commented on the histologic features as being masses of cells with a minimum of patent vessels. The pure type can be mistaken for hemangiosarcoma and is frequently recur-

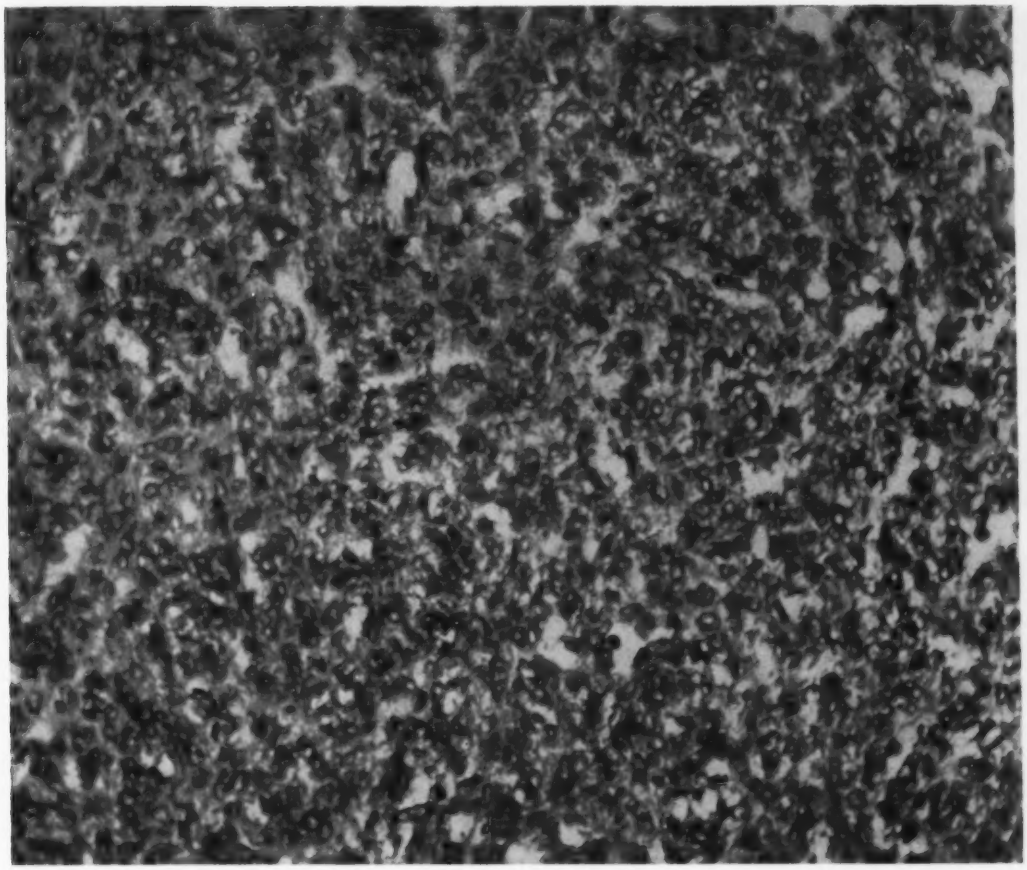

Fig. 3. Microscopic section of the biopsy specimen (×360). The tumor was reported as malignant with hemangioendotheliomatous characteristics.

rent after surgery, which indicates its local aggressiveness.

Stout[4,5] has contributed greatly to the understanding of the pathology of malignant tumors of vascular origin. All are characterized by the formation of vascular channels, but with different cells playing a dominant role in tumor growth. If cells of the inner lining are predominant, we have (a) the hemangioendothelioma; if the muscular layer of the vessel is active, then (b) a leiomyosarcoma results; and, finally, if the tumor originates in cells of the outer surface sheath of the vessel, it is (c) the hemangiopericytoma.

The reticulum stain is of great value in differentiating between hemangioendothelioma and hemangiopericytoma. The silver reticulum stain of the histologic slide will show that all the cells are inside of the reticulum sheaths and are, therefore, endothelia, while the reverse is true for the pericytoma. Besides this, Stout stresses that in a hemangioendothelioma there is formation of atypical endothelial cells in greater numbers than are required to line the vessels with a simple endothelial membrane, formation of vascular channels with a delicate framework of reticulum fibers and a marked tendency for their lumens to anastomose. The pathologic material in the present case was studied by the author with the use of the reticulum stain and it shows the features of a hemangioendothelioma as described by Stout (Fig. 7).

In regard to the malignant qualities of this tumor and the prognosis, several salient features should be emphasized. McCarthy and Pack[2] and Stout[4] have stressed that there is one variety of hemangioendo-

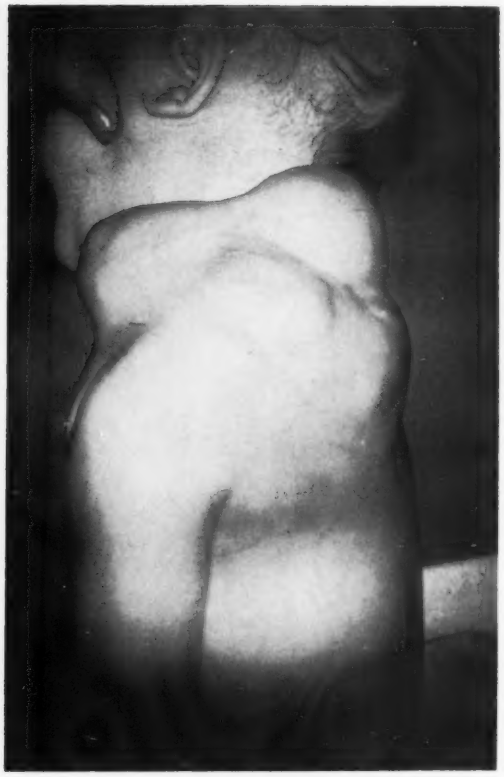

FIG. 4. Left shoulder and back of the infant at ten and one-half months of age, nine months after the initial irradiation and prior to the second course of therapy. Note the areas of tumor regression where the effect of irradiation from the tangential and oblique portals was greatest.

FIG. 5. Anteroposterior view of the chest at the age of one year and five months, or six months after the second course of irradiation. Note the marked decrease of soft tissue tumor, early calcification, and improvement of the thoracic rib deformity. (Compare with Figure 1.)

FIG. 6. The upper back four and one-half years after irradiation. Note the long scar resulting from the incision for the biopsy, and the atrophy or absence of muscles in this area caused by the congenital replacement of any normal musculature by the tumor. The darkening of the skin is exaggerated by a photographic shadow, but irradiation changes are minimal.

thelioma which is seen in infancy or early childhood and which has a rather benign course. McCarthy and Pack caution against the acceptance of the ambiguous term, "hemangioendothelioma," in children. They further state that hemangioendothelioma connotes a highly malignant sarcoma (as our pathologist suggested) and often the surgeon desires to do an amputation, as in our case.

The radiation therapy of hemangioendothelioma of infancy can present difficulties if its proper pathologic identity is not recognized. Many radiotherapists are acquainted with the method and techniques of treating hemangiomas in infants. The chief criteria are early treatment with small doses fractionated over a long interval to supplement or augment the tendency to natural regression or spontaneous remission. The author believes that hemangioendothelioma of infancy, especially the hypertrophic type, should be treated similarly. There is considerable danger if the pathologic state is not recognized and it is interpreted as a form of malignant sarcoma. The surgeon will always do radical surgery and the radiotherapist may be tempted to give a large cancerocidal dose in the usual short interval of four to five

weeks. There will be resulting skin damage and the normal structures will be prevented from developing properly. Since the child will survive long after the radiation has been given, there will be greater dangers of even more serious complications, such as cancer developing in the skin and bone in the long latent period.

If the lesion is large, as it was in our case, it will be advisable to avoid the use of large direct fields. Small multiple tangential fields to avoid the deeper structures are most appropriate. It is necessary to deliver radiation only to a major part of the lesion, since total regression will occur eventually.

From the factors used in this case, a tumor depth dosage can be derived. However, it is difficult to calculate the depth dose accurately since the radiation was directed obliquely and tangentially through multiple small fields to avoid a large dose to the underlying structures. Nevertheless, for theoretical purposes, at a 5 cm. depth in the lesion, and assuming that all the five portals contributed, we may conclude that approximately 2,000 r was delivered to the maximum point and at a 10 cm. depth, a dose of 1,000 r. This was over a period of five weeks. The lesion was observed to have regressed moderately over a ten month period and then a nearly similar course of irradiation was given as described in the case report. The figures cited are maximum values, but in reality they probably were considerably lower. In retrospect, it is probable that a lower dosage would have been utilized if we had better understood the pathologic characteristics and anticipated the degree of radiation response.

The result from the radiation treatment has been most gratifying. There has been very little skin change, and the thoracic rib

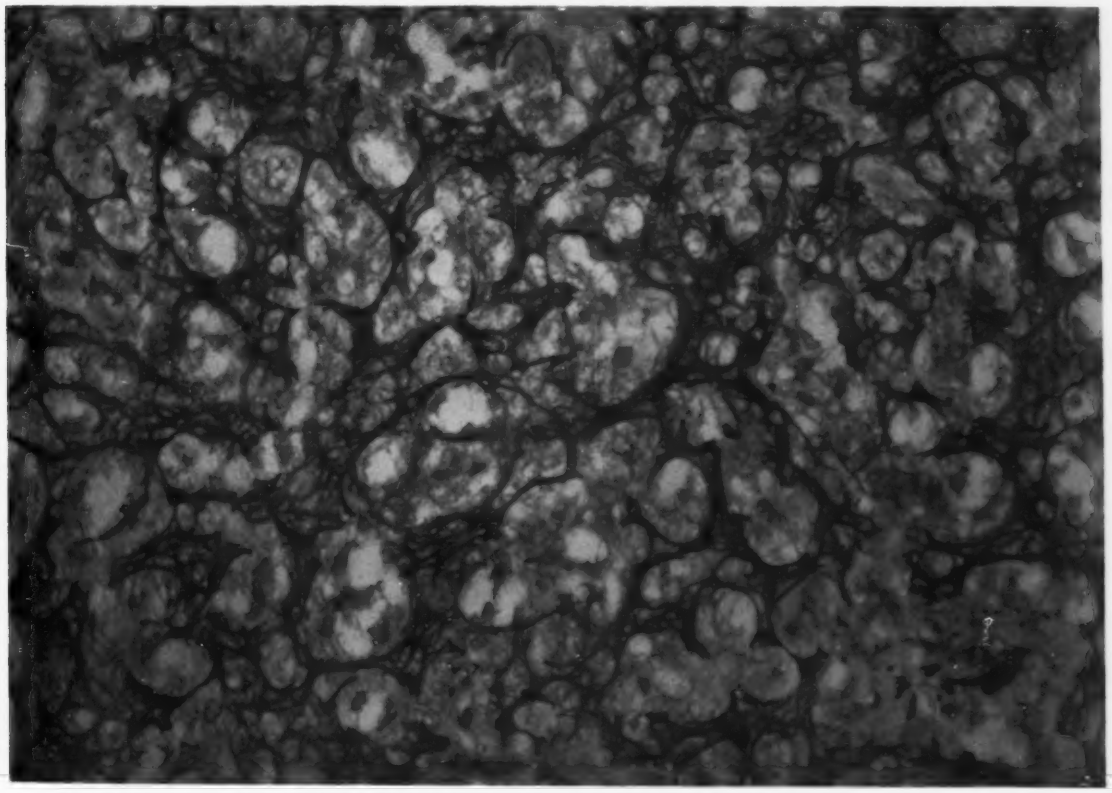

Fig. 7. Microscopic section with a reticulum stain (×315), showing the chracteristic histology of a hemangioendothelioma (Stout). The section demonstrates the great number of endothelial cells lining the lumen of anastomosing vessels.

and vertebral development have been normal (compare Figure 1*A* and Figure 8). Since the tumor originated in or congenitally replaced the left upper spinal musculature, there is a slight atrophy or lack of development in this region following the tumor regression (Fig. 6). Roentgen study shows a normal chest cage (Fig. 8). A moderate amount of calcification has developed in the area of the former tumor (Fig. 9); it is a monument to the history, course, and treatment of this disease. The child is nearing the completion of her fifth year after therapy and there are no indications of any recurrence.

CONCLUSIONS

Proper recognition of this vascular lesion in infancy and early treatment are believed to be essential if radiation therapy is to be used. If we follow Stout's pathologic criteria and also consider the lack of any purpura, the benign course of a hypertrophic lesion in infancy, and the protracted radiation response, the lesion in the infant studied is best classified as a hypertrophic hemangioendothelioma of infancy.

The infant was seventeen days old when therapy was instituted. Radiation dosage should be in a low to moderate range, depending upon the extent and bulk of the lesion. The irradiation should be fractionated over a long period to observe the response and to take advantage of any natural or spontaneous regression that may occur.

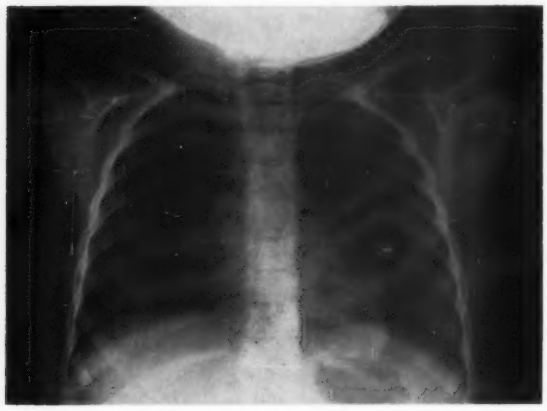

FIG. 8. Anteroposterior view of the chest four years after irradiation. Note the good development of the left upper chest and the calcification in the left supraclavicular region.

FIG. 9. Left oblique view of the shoulder demonstrating calcification at the former site of the tumor.

SUMMARY

1. A case of hypertrophic hemangioendothelioma in a seventeen day old infant is reported. The lesion originated in the left upper thoracic paraspinal musculature.

2. The pathologic and clinical criteria are given for the proper identification of the lesion.

3. Because of the frequently benign nature of this lesion, extensive surgical procedures should be avoided.

4. Radiation dosage should be in the lower range and the course should be protracted to augment a possible natural tendency to regression.

5. The reported child has developed well with no radiation sequelae. The site of the

former tumor shows calcification five years later.

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Dr. Arthur S. J. Petersen was most helpful in suggesting the use of multiple small fields.

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A SIMPLE METHOD OF REDUCING THE FLUOROSCOPIC DOSE RATE

By EDWIN L. LAME, M.D.
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TO IMPLEMENT some of the recent thought on fluoroscopic safety, we started a plan three years ago that has proved most satisfactory and seems easily applicable for all users of modern machines. The roentgen dose rate can be regulated at will for each case and can be so reduced that babies and pregnant women may be examined with hitherto unaccustomed low dosage.

Since, even today, there is evidence that some fluoroscopes are operated by radiologists at high r rates (up to 46 r per minute at table top[4]), it may be useful to review a method that is so simple.

The best fluoroscopic techniques should be in operation in the children's hospitals. Our analysis of current practice in thirteen children's hospitals shows that in orthodox fluoroscopy the kv. peak ranges from 40 to 95, the ma. from 1 to 4, and the r/min. from 1 to 7.5. The average usual kv. peak is 73, the average ma. is 2.5, and the average r/min. is 3.6 (Table 1). This is an enviable record for those using 1 r/min. and we wish to publicize such excellent habits for the information of all radiologists. It would be desirable to reduce the

FIG. 1. Fluoroscopic ma. meter large enough for easy reading and setting.

TABLE I

FLUOROSCOPIC FACTORS USED IN 13 CHILDREN'S HOSPITALS IN THE UNITED STATES

Hospital	Usual			Highest			Lowest		
	kv. peak	ma.	r/min.	kv. peak	ma.	r/min.	kv. peak	ma.	r/min.
1	70	2	1.9	90	3	2.8	60	1	1
2	85	1.5	1.75	95	3	3.2	65	1	1.1
3	70	2.4	1.9	90	2.4	3.1	55	2.4	1.1
4	80	4	3.6	90	4	4.6	65	4	2.1
5	70	2	4.5	80	3	7.5	60	1	2.2
6	85	3	5	95	3	5	55	3	5
7	95	2	2.25	95	3	3.5			
8	60	2	1.66	70	2		50	2	
9	65	3	4	75	3	5		3	
10	70	3	9						
11	55	2		65	2		40	2	
12	74	3		78	3		68	3	
13	80	3		85	3		75	3	

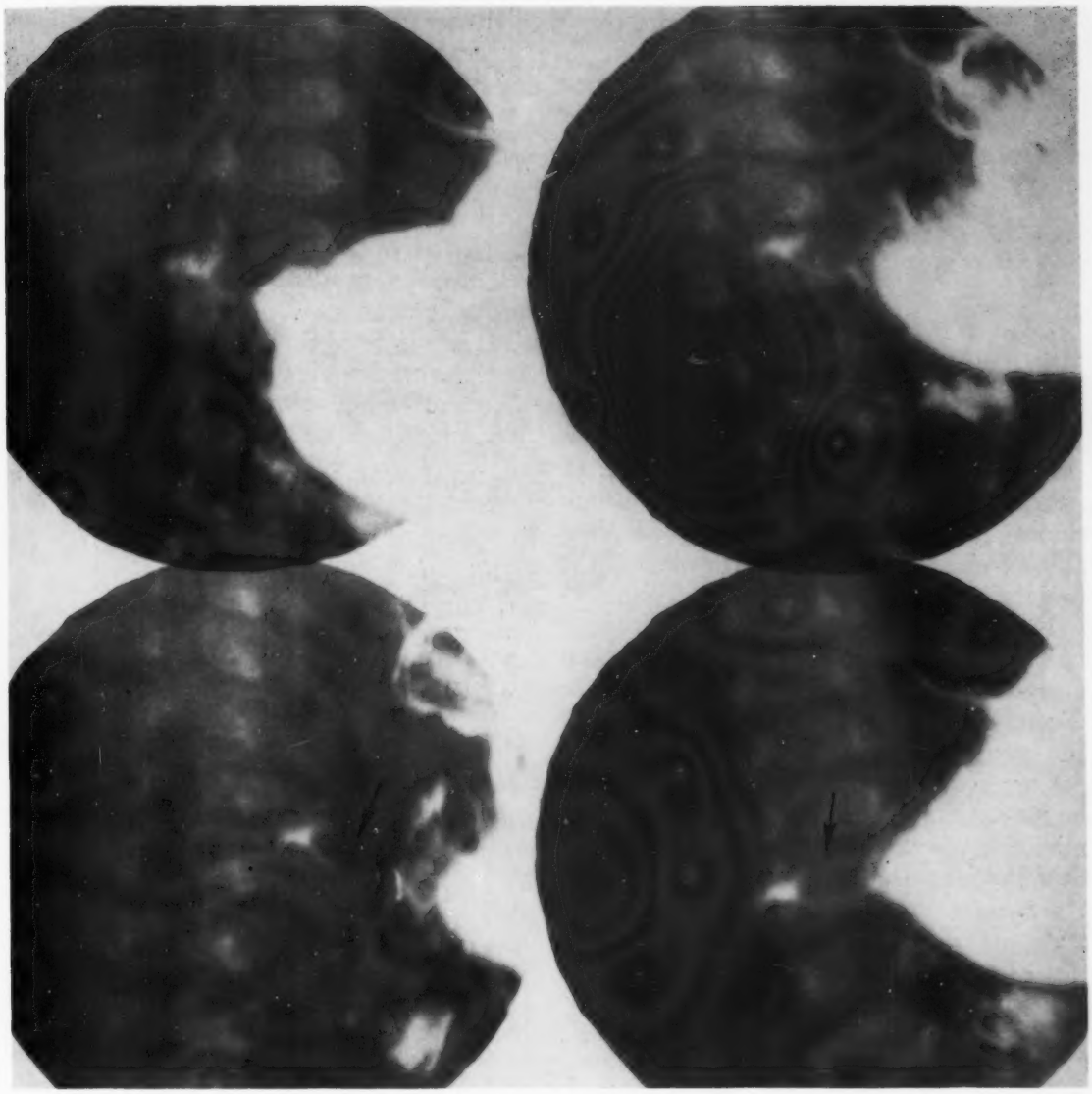

FIG. 2. Roentgenograms made on 8×10 inch film carrying 4 exposures. Diameter of the aperture was 8 cm.

higher rates for children and, further, to offer adults a similarly low exposure approximating the children's dosage. This seems realized in our recent program.

RECOMMENDED METHOD

Most new control panels have a hand regulator of fluoroscopic milliamperage, but manufacturers will equip old panels if requested. This hand regulator is locked at a maximum of 3 ma., forcing the operator to use a higher kv. peak and promptly reducing r output.

Recently, a wide scale milliammeter has been purchased (Fig. 1). It is easy to adjust and read and is much preferred by the physicist, technician and radiologist.

The most gratifying results are in the ability to fluoroscope babies and children or pregnant women with a very low total dose. The calibrating physicist measures the dose at required factors and these dose rates are posted in the technician's booth at each machine. At the start of each fluoroscopic examination the technician asks the radiologist his needs for voltage

and current. Sample readings from our 3 machines are as follows:

kv. peak	ma.	r per minute		
60	0.5	0.95	1.0	0.7
60	1	1.53	1.8	1.2
70	1	2.14	2.6	1.6
85	1	3.4	3.5	2.2
85	2	4.76	6.4	3.5
90	2	5.8	7.7	5.1
90	3	6.7	9.8	7.0

Reference to the operating factors above makes it evident that an infant can be examined at 60 kv. peak and 0.5 ma. for an r rate of 0.7 to 1.0 per minute. Our barium fluoroscopy for an infant usually is limited to 1 minute and hence a dose of about 1 r is maintained.

Further reduction of total body dose for babies is effected by using the 8 cm. diameter 4 on 1 spot filmer as a fixed aperture during all of the fluoroscopy and most of the roentgenography (Fig. 2).

Correspondingly, thin adult chests can be examined at dose rates of 1.6 to 2.6 r per minute (70 kv. peak-1 ma.). Adult barium examinations are done at 85 kv. peak and 1 ma. for thin patients, 85 to 90 kv. peak and 2 or 3 ma. for heavier patients (dose rate of 2.2 to 9.8 r/min.).

Comparison with image amplifier dose rates commonly used is most favorable. Most users of the amplifiers do not accomodate their eyes, so that their rates of exposure are the same as ours for children and light-weight adults, and sometimes higher for babies.

SUMMARY

A simple and very inexpensive plan is described of reducing roentgen dose rate in fluoroscopy. It has provided the author with the means for examining delicate tissues that otherwise would be rejected for fluoroscopy or overdosed by current standards of safety.

It is suggested that this method is worthy of wider trial in view of the continued prevalence of more robust fluoroscopic examination.

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EDITORIAL

THE THYMUS GLAND IN CHILDREN AND THE ROENTGENOLOGIST

PROBLEMS related to the thymus gland in children continue to provide grounds for speculation and controversy. The general roentgenologist does not have as frequent an opportunity to familiarize himself with thymic disease as does the pediatric roentgenologist. Nevertheless, he does encounter recurring experience with two basic problems. The first is a diagnostic question: Is the thymus gland enlarged? The second is a therapeutic problem: Should the thymus be treated by radiation? A historical survey of the roentgenologist's association with the thymus gland helps to elucidate our present role.

Medical knowledge of the presence of the thymus gland probably dates from antiquity. In an extensive review, Marine[1] credited Felix Plater with introducing in 1614 the concept of sudden death in children due to an enlarged thymus gland. In 1889 Paltauf[2] focussed new interest on the thymus gland by introducing the idea of a constitutional disease, status thymicolymphaticus, consisting of hyperplasia of the lymphoid structures including the thymus, arterial hypoplasia, chlorosis, and a tendency to unexplained sudden death.

Only eight years after Röntgen's discovery of the x-ray, Heineke[3] described the effects of the x-ray on lymphoid tissue in experimental animals and suggested that such therapy might have value in human beings with abnormally large thymus glands. Friedlander[4] put this hypothesis to trial in 1905, when he treated an infant with a respiratory ailment thought to be due to thymic stridor and status lymphaticus. By this time it was widely believed that these patients responded poorly to anesthetic drugs and suffered a high rate of sudden, unexpected death. That radiation was increasingly accepted as a useful means of controlling the enlarged thymus and its feared consequences is readily attested by a review of early volumes of the AMERICAN JOURNAL of ROENTGENOLOGY.

In a report of 41 cases in 1920, Heublein[5] gave the reasons why radium therapy was considered even more useful than roentgen therapy. Grier[6] agreed that radium was easier and safer to use; his report is notable because it emphasized also the responsibility of the roentgenologist in the diagnosis of the enlarged thymus. In a roentgenographic study, he stressed the importance of the phase of respiration, the increased size of the thymic shadow when the child cries, and the tendency of the shadow to be bilateral, relatively symmetric, and wider inferiorly. Writing at a still later date, Köhler[7] described graphically the difficulty encountered by earlier diagnosticians: "In the first decade after Röntgen, enlargement of the thymus was far too frequently diagnosed, the striking breadth of the upper part of the central shadow being due to the tube being brought too near, in order to take a more rapid picture of small unruly children. . . ."

[1] MARINE, D. Status lymphaticus. *Arch. Path.*, 1928, *5*, 661–662.

[2] PALTAUF, A. Cited by Friedlander.[4]

[3] HEINEKE, H. Ueber die Einwirkung der Röntgenstrahlen auf innere Organe. *München. med. Wchnschr.*, 1904, *51*, 785–786.

[4] FRIEDLANDER, A. Status lymphaticus and enlargement of the thymus. With report of a case successfully treated by the x-ray. *Arch. Pediat.*, 1907, *24*, 490–501.

[5] HEUBLEIN, A. C. Radiation treatment of enlarged thymus glands in infants. AM. J. ROENTGENOL. & RAD. THERAPY, 1920, *7*, 191–195.

[6] Grier, G. W. The diagnosis and treatment of enlarged thymus. AM. J. ROENTGENOL. & RAD. THERAPY, 1924, *11*, 141–146.

[7] KÖHLER, A. Roentgenology: The Borderlands of the Normal and Early Pathological in the Skiagram. Second English Edition. Wm. Wood & Co., Baltimore, 1935, p. 477.

The popularity of radiation therapy met some resistance. In 1927 Greenwood and Woods[8] described the whole concept of status thymicolymphaticus "as a good example of the growth of medical mythology." Opposing thymic irradiation, Kennedy and New[9] reported that chronic stridor and other symptoms commonly attributed to an enlarged thymus were usually due to causes unrelated to the thymus. In general, however, roentgenologists and other physicians diagnosed and treated an increasing number of large thymus glands. The peak of this fad was reached in the late 1930's, when many children were treated whether they had symptoms or not. In the 1940's, doubts began to develop about the importance of status thymicolymphaticus, but supposedly symptomatic thymus glands were still subjected to radiation therapy with few qualms about the danger involved.

With the advent of the atomic era and the cataclysmic events at Hiroshima in 1945, the uses of radiation therapy underwent thoughtful reappraisal. Coming under particular scrutiny was its use in children, women in the child-bearing age, and persons having benign diseases. In 1949, Scharnagel and Pack[10] reported the appearance of hundreds of basal cell epitheliomas in the skin of a five year old boy whose enlarged thymus had been irradiated shortly after birth. In 1950, Duffy and Fitzgerald,[11] and, five years later, Clark[12] recorded cases of children with thyroidal cancer, which they associated in many instances with irradiation that had been given during infancy to the thymus or to other benign conditions of the upper trunk. In this same period Dameshek[13] and Simpson and coworkers[14] were pointing out the possibility that leukemia might be associated with irradiation of the thymus in children.

Medical contributions such as these certainly reduce the enthusiasm for irradiation of the thymus gland. During the last decade, also, in some nonradiologic quarters near-hysteria has existed about the observed or projected hazards of radiation damage. Insofar as these developments lead to fuller assessment of our knowledge and to wiser use of radiation therapy, they must be accepted as good. This greater awareness of certain disadvantages, however, should not blind us to the usefulness of radiation therapy, judiciously employed. Recent conscientious studies of large series of patients[15,16] indicate suggestive evidence that thymic irradiation in children may potentially be harmful. A still larger study[17] indicates that it may be a contributing factor to development of cancer of the thyroid. In a similar report by Conti and others,[18] which did not disclose a relationship in the development of either leukemia or thyroidal neoplasm, very small ports (4×4 cm.) were used directly over the thymus. This report states that careful, limited irradiation of the thymus may be undertaken without undue risk. The roentgenologist may observe in these reports an interesting telltale—that the departments from which the studies originate have largely abandoned use of irradiation for benign thymic enlargement.

The answer to our first question, then,

[8] Greenwood, M., and Woods, H. M. "Status thymicolymphaticus" considered in light of recent work on thymus. *J. Hyg.*, 1927, *26*, 305–326.

[9] Kennedy, R. L. J., and New, G. B. Chronic stridor in childhood sometimes erroneously attributed to enlargement of the thymus. *J.A.M.A.*, 1931, *96*, 1286–1289.

[10] Scharnagel, I. M., and Pack, G. T. Multiple basal cell epitheliomas in a five year old child. *Am. J. Dis. Child.*, 1949, *77*, 647–651.

[11] Duffy, B. J., Jr., and Fitzgerald, P. J. Thyroid cancer in childhood and adolescence. Report on 28 cases. *Cancer*, 1950, *3*, 1018–1032.

[12] Clark, D. E. Association of irradiation with cancer of the thyroid in children and adolescents. *J.A.M.A.*, 1955, *159*, 1007–1009.

[13] Dameshek, W. The outlook for the eventual control of leukemia. *New England J. Med.*, 1954, *250*, 131–139.

[14] Simpson, C. L., Hempelmann, L. H., and Fuller, L. M. Neoplasia in children treated with x-rays in infancy for thymic enlargement. *Radiology*, 1955, *64*, 840–845.

[15] Snegireff, L. S. The elusiveness of neoplasia following roentgen therapy for thymic enlargement in children. *Radiology*, 1959, *72*, 508–517.

[16] Latourette, H. B., and Hodges, F. J. Incidence of neoplasia after irradiation of thymic region. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1959, *82*, 667–677.

[17] Saenger, E. L., Silverman, F. N., Sterling, T. D., and Turner, M. E. Neoplasia following therapeutic irradiation for benign conditions in childhood. *Radiology*, 1960, *74*, 889–904.

[18] Conti, E. A., Patton, G. D., Conti, J. E., and Hempelmann, L. H. Present health of children given x-ray treatment to the anterior mediastinum in infancy. *Radiology*, 1960, *74*, 386–391.

is: a prominent thymus may be discovered, but its significance is doubtful. The roentgenologist must diagnose its presence and perhaps follow its involutional course in children, but should not produce undue alarm in reporting its size or supposed effect upon the trachea.

In answering the question about therapy, the roentgenologist must almost certainly accept the idea that radiation therapy for an enlarged thymus is rarely advisable. This change in emphasis is as much a product of modern knowledge about normal variations of the gland, the infrequency of pressure symptoms, and the vanishing concept of status lymphaticus as it is of concern about the possible association of subsequent thyroidal or lymphoid cancer. However, if a large thymus is obstructing respiration in a child in whom complete pediatric and otolaryngologic appraisal reveals no other cause, use of *small* doses of roentgen therapy to a *small* portal below a carefully shielded thyroid gland is justified.

Based on an appraisal of general statistics indicating a continued low incidence of thyroidal cancer in children, and a long, personal experience in irradiation of children, Garland[19] believes that "An etiological connection between low-dose neck irradiation and subsequent thyroid cancer is not regarded as established."

Seymour Fiske Ochsner, M.D.

Ochsner Clinic
Prytania and Aline Streets
New Orleans 15, Louisiana

[19] Garland, L. Henry. Cancer of the thyroid and previous irradiation. *Surg., Gyn. & Obst.*, 1961, *112*, 564–566.

NEWS ITEMS

DR. OTTO GLASSER HONORED

To Otto Glasser, Ph.D., teacher, leader and friend to the radiologist of Ohio, the members of the Ohio State Radiological Society presented a scroll in recognition of his many contributions to Radiology. Also, in appreciation of these and his many other attainments as author and investigator in the field of biophysics, the Ohio State Radiological Society on May 20, 1961 conferred upon him an Honorary Membership.

THE ASSOCIATION OF UNIVERSITY RADIOLOGISTS

Annual Memorial Medal Award Competition

The Association of University Radiologists has recently established an annual Memorial Medal Award in honor of deceased members, to be awarded to the resident in radiology writing the best original paper on some aspect of radiology during the period of competition. The paper must be the work of a single author, the resident. Manuscripts to be considered for the 1962 competition must be received by March 1, 1962. Inquiries should be addressed and papers submitted to the Secretary, Herbert M. Stauffer, M.D., Department of Radiology, Temple University Medical Center, Philadelphia 40, Pennsylvania.

The 1961 Memorial Medal Award was won by Dr. Burton Seife, Resident, Yale University, for his paper, "Radioactive Inert Indicator Method for Intestinal Absorption Utilizing Differential Counting," presented at the recent meeting of the Association at Stanford University Medical Center, Palo Alto, California.

The 1962 annual meeting will be held at the University of Indiana in Indianapolis, May 19 and 20.

JAMES PICKER FOUNDATION

Awards for 1961–1962

On behalf of the James Picker Foundation, the National Academy of Sciences-National Research Council announces the award of twenty-five grants and fellowships in the field of radiology and nuclear medicine for 1961–1962. These awards, totaling approximately $150,000, were recently approved by the Foundation on recommendation of the Committee on Radiology of the Academy-Research Council. With the advice and cooperation of the Committee, the Foundation inaugurated its research grants and fellowships in 1950, with the objective of fostering research in, and broadening the scope of radiology. During the past year, the program was expanded to include a new series of Advanced Fellowships in Academic Radiology, in recognition of the increasing interest of the Foundation in the advancement of medical education. The first three of these Fellowships, designed to assist young radiologists who are preparing for careers as medical school teachers, have been awarded for 1961–1962.

At the same time, the National Research Council of Canada announces on behalf of the Foundation the award of two Research Grants for the coming academic year. Since 1958, the Canadian National Research Council has served as scientific adviser to the James Picker Foundation with respect to its Canadian program.

Including the awards for the coming year, during the eleven year period research grants have been made through the U. S. Academy-Research Council for support of seventy-one investigations throughout the world. Twenty-five universities and nine hospitals and research laboratories within the Unites States have received grants. Investigators in four Canadian institutions were awarded support before the Canadian National Research Council assumed responsibility for the Foundation's Canadian program in 1958. Grants have been made to ten institutions in seven countries abroad. Nine Scholars in Radiological Research have been supported in nine universities in this country.

Research Fellowships have been awarded to twenty-six young scientists to enable them to prepare for investigative careers in the field of radiology. Fifteen of these fellows were citizens of countries other than the United States, and eleven of the latter studied in this country or Canada. Three of the Americans have carried on their research in England and Sweden.

The Canadian National Research Council since 1958 has administered ten Research Grants in Canadian institutions, and has recommended the award of one Research Fellowship in Canada.

JAMES PICKER FOUNDATION

Application for Awards for 1962–1963

On behalf of the James Picker Foundation, the National Academy of Sciences-National Research Council is accepting applications for fellowships and grants in the field of radiology and nuclear medicine for the year 1962–1963. Awards are made in four categories:

The Advanced Fellowships in Academic Radiology. The purpose is to prepare the fellow to meet in full the intellectual demands of an academic position in radiology. Preference will be given to applicants under thirty-four years of age. Completion of clinical training in radiology ordinarily will be a prerequisite. The candidate should be prepared to devote a minimum of two years to course work in the basic sciences and to the application of the techniques and methods of these basic disciplines to radiological research. In arranging the details of his program, the prospective fellow will have opportunity for consultation with members of the Academy-Research Council's Committee on Radiology. Applications will be accepted on nomination by a clinical adviser, who should be a member of the staff of a department of radiology in a medical school.

Postdoctoral Research Fellowships are open to recent graduates who desire investigative experience and training in radiology or nuclear medicine. Applicants must hold the M.D., Ph.D. or Sc.D. degree or the equivalent. Awards are for a period of one year, but requests for renewal will be considered.

Grants for Scholars are offered to assist medical schools in supporting and developing junior staff members in radiology. This is a transitional form of support, designed to bridge the gap between the completion of research fellowship training and the period when the young scientist has thoroughly demonstrated his competence as an independent investigator. The application is submitted by the institution on behalf of the prospective Scholar. If the request is approved, a grant of $6,000 per year will be made directly to the institution as a contribution toward the Scholar's support or his research, or both. Initial grants are made for two years, but renewal for a third year may be recommended.

Grants-in-Aid of Research are designed to encourage investigations in radiology and nuclear medicine offering promise of improvement in methods of diagnosis or treatment of disease. Radiological studies involving the use of radioisotopes fall within the scope of this program. Research grants are awarded to institutions, rather than to individuals. Initial awards may be made for two years.

Applications for the fiscal year 1962–1963 should be submitted by October 1, 1961. Support is not restricted to citizens of the United States or to institutions within this country. Application blanks and further details may be obtained from the *Committee on Radiology, National Academy of Sciences-National Research Council, 2101 Constitution Avenue, N.W., Washington 25, D. C.*

The Medical Research Council of Canada serves as scientific adviser to the James Picker Foundation with respect to its Canadian program. If the proposed studies are to be carried out in Canada, requests for information and application forms should therefore be directed to the Secretary, Medical Research Council, National Research Building, 100 Sussex Drive, Ottawa 2, Canada.

SPECIAL PROGRAM FOR RESEARCH GRANTS IN RADIOLOGICAL HEALTH

A greatly expanded program for research grants in the field of radiological health has been developed by the U. S. Department of Health, Education, and Welfare, Public Health Service, Division of Radiological Health. These grants are offered to support research by individuals, universities, hospitals, laboratories, and other public or private institutions in the assessment and control of manmade and natural radiation exposures to the individual, no matter how the separate components may originate. The knowledge and skills of many professional disciplines and specialties—physicians, engineers, physicists, chemists, educators, statisticians among them—are needed to find answers to the many challenging questions in radiological health.

Basic studies relating to critical body organs and systems, preferred metabolic pathways for specific radioactive contaminants and an understanding of the radiosensitizing and modifying effects of various materials are encouraged. Broad epidemiological studies aimed at a scientific evaluation of the long term effects such as aging, congenital malformations, genetic effects, behavioral patterns, and cancer induction are also of primary concern. Field studies of the movement of radioactive contaminants in biota and human food chains are of special interest, since the physical environment may be greatly altered by biological activity, as for example, the concentration of waterborne radionuclides in microorganisms and fish. Purely physical studies, such as chemical mechanisms in radiation chemistry, the design of equipment and the development of techniques to accurately assess or reduce the population dosage are mandatory for a successful research program.

For information and/or application forms please contact: Dr. Paul F. Hahn, Chief, Office of Extramural Grants, Division of Radiological Health, U. S. Public Health Service, Washington 25, D. C.

OPERATIVE RADIUM THERAPY DAY AT QUEENS HOSPITAL CENTER

An Operative Radium Therapy Day is to be given at the Queens Hospital Center by the Radiation Medicine Department on Wednesday, October 18, 1961.

The program will include the use of interstitial radiation in the oral cavity; radical insertion of radium in the neck; various applicators in carcinoma of the cervix; the Heyman applicators in carcinoma of the endometrium; radium needles in the parametria; and radon, iridium-thread, and cobalt interstitial therapy. Clinical demonstration will depend on availability of patients.

The enrollment is limited and the registration fee is $10.00.

Please apply to: Dr. Philip J. Kahan, Supervising Medical Superintendent, Queens Hospital Center, 82–68 164th Street, Jamaica 32, N. Y.

BOOK REVIEW

Books sent for review are acknowledged under: Books Received. This must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interest of our readers as space permits.

Strahlenbiologie, Strahlentherapie, Nuklearmedizin und Krebsforschung; Ergebnisse 1952–1958. Edited by H. R. Schinz; H. Holthusen; H. Langendorff; B. Rajewsky; and G. Schubert. Cloth. Price, $65.50. Pp. 998, with numerous illustrations and tables. Georg Thieme Verlag, Herdweg 63, Stuttgart, Germany, 1959. In the U.S.A. and Canada, Intercontinental Medical Book Corporation, New York 16, N. Y.

German medical literature has demonstrated the successful use of "Ergebnisse" for a long time, *i.e.*, a collection of chapters written by different authors and pertaining to different fields of medicine. This volume is the first of its kind in the field of radiation biology, radiation therapy, nuclear medicine and cancer research. It comprises 16 different chapters, varying in length from 12 to 90 pages. There are purely scientific chapters, such as those dealing with the radiation genetics of bacteriophages, of micro-organisms, of Drosophila, and of mammals. Other chapters in the field of radiation physics are concerned with problems of dosage, and the physics and technique of megavolt radiation. The greater part of the book deals with practical aspects of radiation therapy, such as experience with the 31 megavolt betatron and intravesical radiocobalt therapy in Zurich, radiation therapy of bronchogenic carcinoma, a critical review of therapy with radioactive isotopes, clinical diagnosis of diseases of the thyroid by means of radioiodine, and others. The authors contributing to this book are working in Switzerland and Germany.

Every chapter has a very extensive bibliography for the years 1952–1956 which should be of considerable assistance to anyone who is interested in a special phase of radiation biology or radiation therapy.

There are excellent illustrations and the print is of high quality.

For a practicing radiologist who can read German, the book is of considerable interest for a general review of basic biologic and therapeutic radiation problems. Some of the chapters may not be applicable for a busy practitioner of radiology, since they pertain to rather specific biologic radiation effects. The chapters on therapeutic radiology, however, are excellent reading for the radiation therapist who wishes to acquaint himself with the broad field of new means of irradiation as practiced in mid-European clinics and centers. The world literature pertaining to these separate fields (especially publications from the United States, all other European countries and Russia) is well assimilated and incorporated into the review of these special aspects of radiation biology and therapy. This book is highly recommended and should be available in any larger medical library as well as in the library of the radiobiologist or radiotherapist who can read German.

Hans W. Hefke, M.D.

BOOKS RECEIVED

Vertebral and Carotid Angiograms in Tentorial Herniations; Including Roentgen Anatomy of the Tentorial Incisure. By Hans F. Plaut, M.D., Chief, Radiology Service, Veterans Administration Center, Dayton, Ohio; Clinical Assistant Professor of Radiology, Ohio State University, College of Medicine, Columbus, Ohio; and Formerly, Instructor in Radiology, University of Cincinnati College of Medicine, Cincinnati, Ohio. Cloth. Price, $10.50. Pp. 155, with many illustrations. Charles C Thomas, Publisher, 301–327 East Lawrence Avenue, Springfield, Ill., 1961.

A Manual for Nuclear Medicine. By E. R. King, Captain, MC, U. S. Navy; and T. G. Mitchell, Lieutenant, MSC, U. S. Navy. Cloth. Price, $13.50. Pp. 406, with 80 illustrations. Charles C Thomas, Publisher, 301–327 East Lawrence Avenue, Springfield, Ill., 1961.

Phlebography and Venous Pressure Determination; A Study into the Correlation of the Data Gained from These Methods. By M. N. Van Der Heyde, M.D. Cloth. Price, $5.00. Pp. 83, with 23 illustrations. Charles C Thomas, Publisher, 301–327 East Lawrence Avenue, Springfield, Ill., 1961.

Bronchographie Clinique. By Étienne Bernard, Professeur de Clinique de Pneumo-Phtisiologie à la Faculté de Médecine de Paris, Médecin de l'Hôpital Laënnec; and Bernard Gamain, Chef de Laboratoire à la Faculté de Médecine de Paris, Assistant de l'Hôpital Laënnec. Paper. Pp. 196, with 132 illustrations. Masson et Cie, Éditeurs. 120

Boulevard Saint-Germain, Paris (6e), France, 1961.

Die juvenilen Rückgratverkrümmungen. By Priv.-Doz. Dr. Med. Friedrich Wilhelm Rathke, Heidelberg. Cloth. Price, $5.90. Pp. 156, with 122 illustrations. Georg Thieme Verlag, Herdweg 63, Stuttgart, Germany, 1961. In the U.S.A. and Canada, Intercontinental Medical Book Corporation, New York 16, N. Y.

Hartstrahltechnik. By Dr. Med. Wolfgang Frik, Privatdozent der Med. Strahlenkunde, Med. Klinik mit Poliklinik der Universität Erlangen. Paper. Price, $7.15. Pp. 144, with 76 illustrations. Georg Thieme Verlag, Herdweg 63, Stuttgart, Germany, 1961. In the U.S.A. and Canada, Intercontinental Medical Book Corporation, New York 16, N. Y.

Die Präoperative Röntgenbestrahlung des Mammakarzinoms. By Dr. E. Muntean, Universitätsdozent, Graz. Paper. Price, $4.40. Pp. 108, with 9 illustrations and 26 tables. Georg Thieme Verlag, Herdweg 63, Stuttgart, Germany, 1961. In the U.S.A. and Canada, Intercontinental Medical Book Corporation, New York 16, New York.

Éléments de Radiobiologie Appliquée. By Roland Buchet, Médecin Radiologiste des Hôpitaux de Paris; avec la collaboration de G. Breitman, Attaché d'Électroradiologie des Hôpitaux de Paris. Paper. Pp. 189, with 127 illustrations. Masson et Cie, Éditeurs, 120 Boulevard Saint Germain, Paris (6e), France, 1960.

Acta Orthopaedica Scandinavica. Supplementum No. 43. Lumbar Intradiscal Pressure; Experimental Studies on Post-mortem Material. By Alf Nachemson. Paper. Pp. 104, with illustrations and tables. Ejnar Munksgaard, Copenhagen, Denmark, 1960.

Acta Orthopaedica Scandinavica. Supplementum No. 45. The Effects of Subperiosteallay Implanted Autogenous Whole-Thickness Skin Graft on Growing Bone; An Experimental Study. By Jaakko O. Elo. Paper. Pp. 90, with many illustrations and tables. Ejnar Munksgaard, Copenhagen, Denmark, 1960.

Acta Orthopaedica Scandinavica. Supplementum No. 46. The Surgical Anatomy and Pathology of the Supraspinous and Interspinous Ligaments of the Lumbar Spine with Special Reference to Ligament Ruptures. By Pentti M. Rissanen. Paper. Pp. 100, with 57 illustrations. Ejnar Munksgaard, Copenhagen, Denmark, 1960.

Acta Radiologica. Supplement No. 201. risa Encephalography and Conventional Neuroradiologic Methods; A Comparative Study. By Giovanni Di Chiro. Paper. Price, Sw.Kr. 35:–. Pp. 102, with many illustrations and tables. Acta Radiologica, Box 2052, Stockholm 2, Sweden, 1961.

ABSTRACTS OF RADIOLOGICAL LITERATURE

Department Editor: T. Leucutia, M.D., Harper Hospital, Detroit 1, Michigan

INDEX TO ABSTRACTS

ROENTGEN DIAGNOSIS

Head

Thiébaut, F., Wackenheim, A., and Vrousos, C.: New data on median sagittal pneumostratigraphy of the posterior fossa 608
Spitzer, R., Rabinowitch, J. Y., and Wybar, K. C.: A study of the abnormalities of the skull, teeth and lenses in mongolism 608
Blatt, N. *et al.*: Alterations of the optic canal in Crouzon's disease (craniofacial dysostosis) 608
Legré, J., Denizet, D., and Savelli, J.: Cranial lacunae secondary to trauma suffered in early childhood 609
Hurxthal, L. M.: Pituitary gigantism in a child five years of age: effect of x-radiation, estrogen therapy and self-imposed starvation diet during an eleven-year period 609
Wisoff, H. S., and Rothballer, A. B.: Cerebral arterial thrombosis in children; review of literature and addition of two cases in apparently healthy children 609
Meyer, H.-St., Busch, G., and Dörffel, E. W.: Contribution to the problem of "pseudotumor cerebri" and an intracerebral calcification 610
Worst, J. G. F.: A röntgen reference contact lens, fixed by low vacuum 610

Neck and Chest

Issa, P.: Ventricular laryngocele (report of 4 cases) 610
Dalith, F.: Calcification of the aortic knob: its relationship to the fifth and sixth embryonic aortic arches; a radiological and anatomical study 611
Scheminzky, F., and Schröcksnadel, H.: Influence of radium emanation upon pulse and blood pressure 612
von Bramann, C.: The surgical treatment of primary and secondary reflux esophagitis 612

Abdomen

Healey, W. V. *et al.*: An experimental method for localizing the source of intestinal bleeding 612
Dallos, A.: Complete intestinal obstruction by Meckel's diverticulum 612
Elkan W.: Two rare tumors of the ileum 613
Margulis, A. R., and Mandelstam, P.: The use of parenteral neostigmine in the roentgen study of the small bowel 613
Griffiths, J. D.: Extramural and intramural blood-supply of colon 614
Khilnani, M. T.: Calcified liver metastasis from carcinoma of the colon 614
Sichel, D., Wolff, R., and Eisenbeth, R.: Detection and incidence of benign tumors of the gallbladder (study of 20 cases) 614
Lauchenaur, C.: Prophylaxis of biligrafin reactions 615
Lamprecht, W.: Pancreatic cysts in modern surgery 615

Gynecology and Obstetrics

Singleton, E. B., Rosenberg, H. M., and Samper, L.: Radiologic considerations of the perinatal distress syndrome 615

Genitourinary System

Rutner, A. B., and Smith, D. R.: Renal papillary necrosis 616
Klein, R. L., and McChesney, J. A.: Hypertension secondary to aneurysm of the renal artery: report of a case of long duration cured by nephrectomy 616
Winter, C. C.: Advances in the radioisotope renogram test 617
MacLaurin, J. C., and Arneil, G. C.: Phaeochromocytoma causing ureteric obstruction in a child 617

Nervous System

Schober, R.: The formation of cysts in the coverings of the spinal cord 618

Skeletal System

Innes, J., and Newall, J.: Myelomatosis 618
Unander-Scharin, L.: Melorheostosis; report of a case 619
Naide, M., and Schnall, C.: Bone changes in necrosis in diabetes mellitus; differentiation of neuropathic from ischemic necrosis 619

Hansen, H.-J., and Ullberg, S.: Uptake of S^{35} in the intervertebral discs after injection of S^{35}-sulphate. An autoradiographic study. 619

Andrén, L., and Wehlin, L.: Double-contrast arthrography of knee with horizontal roentgen ray beams. 620

Blood and Lymph System

Mones, R.: Vertebral angiography; an analysis of 106 cases. 620

ROENTGEN DIAGNOSIS

HEAD

THIÉBAUT, F., WACKENHEIM, A., and VROUSOS, C. Nouvelles données de la pneumostratigraphie sagittale médiane de la fosse postérieure. (New data on median sagittal pneumostratigraphy of the posterior fossa.) *J. de radiol., d'électrol. et de méd. nucléaire*, Feb., 1961, *42*, 1–7. (From: Laboratoire de Radiologie de la Clinique neurologique de Strasbourg, France.)

In an earlier article published in the same journal in 1959, the authors described the laminagraphic technique applied to the study of the vermis cerebelli during a pneumoencephalographic examination. The normal and pathologic roentgen anatomy of this region is important in order to recognize some neurologic diseases and malformations, and to avoid unnecessary surgical exploration.

Three points are mentioned concerning the normal anatomy as seen roentgenographically: (1) dilatation of the postpyramidal groove is considered a normal variant in the absence of cerebellar symptoms and is not a sign of atrophy of the inferior vermis. It forms an accessory inferior cerebellar lobe containing the pyramis, the nodulus, the uvula and the tonsil; (2) the shadow of the vertebral artery is projected as an opaque curl in the foramen magnum and may be seen if the section is paramedian; and (3) diverticular dilatation of the vallecula may be seen in the posteroinferior part of the fourth ventricle.

In the pathologic roentgen anatomy, the authors first report some congenital malformations of the vermis. In agenesis of the inferior vermis, the superior part of the vermis (culmen) shows normal lobulation and the inferior part is hypoplastic and free of furrow formations, with an enlargement of the posterior cerebellar cistern. The authors have observed 5 of these cases which did not show cerebellar symptoms. In cases of Arnold-Chiari malformation with absence of the vermis, this absence may be predicted if the normal anterior transverse groove is not visible on the median convexity of the cerebellum and if, then, the furrows of the cerebellar convexity are seen as the spokes of a wheel, replacing the vermis. This absence of the vermis is also encountered in a rare malformation, cyclocerebellum, which is accompanied by other cerebral malformations.

Secondly, the authors discuss cerebellar atrophy. To distinguish hypoplasia of the vermis from an acquired atrophy, they believe that in the latter case the normal furrows are still present but are enlarged passively by parenchymal retraction. They report cases of cerebrocerebellar atrophy in which the atrophy of the vermis was either silent or clinically symptomatic. In 2 cases, they observed a combination of cortical parietal atrophy and atrophy of the vermis. In 1 of these 2 cases, the pneumoencephalographic signs of the cerebral atrophy were on the side opposite to the cerebellar atrophy.

In conclusion, the authors state that the laminagraphic studies permit recognition *in vivo* of some normal anatomic variants and malformations of the cerebellar vermis.—*H. P. Lévesque, M.D.*

SPITZER, R., RABINOWITCH, J. Y., and WYBAR, K. C. A study of the abnormalities of the skull, teeth and lenses in mongolism. *Canad. M.A.J.*, Mar. 18, 1961, *84*, 567–572. (Address: 3, Prince's Court, Brompton Road, London, S.W.3, England.)

A study was made of the dentition and lenses of 33 mongoloids and of the roentgen appearance of the skulls of 29 mongoloids who were patients at Leavesden Hospital, Herts, England. Their ages ranged from eight to forty-nine years.

There were no roentgen or clinical findings pertaining to the skull, teeth or lenses that were present in all cases. However, there was extreme thinness of the cranium (94 per cent); failure of development of the frontal sinuses (84 per cent); a high percentage of impaired development of *all* paranasal sinuses and mastoids; a high percentage of hypoplasia of the facial skeleton; dental changes, primarily microdontia and anomalies of shape (86 per cent); and a high percentage of lens opacities (23–85 per cent) of three main types, the percentage varying according to the type of opacification. There were other anomalies found less frequently.

The information gained from this study reveals that the anomalies do not occur sporadically, but form a pattern of defects. Since the defects involve a large range of tissues of different derivation, this suggests that the anomalies have been impressed on the developing fetus by genetic endowment rather than by prenatally acquired factors. The facts are suggestive of an inherent fault in the anlage of the structures affected, causing prenatal developmental interference.—*Gerald Davis, M.D.*

BLATT, NICOLAS, ZAMFIR, D., ATANASIU, M., and SLOBOZIANU, H. (Bucarest, Romania.) Les altérations du canal optique dans la maladie de Crouzon (dysostose craniofaciale). (Alterations of the optic canal in Crouzon's disease [craniofacial dysostosis].) *J. de radiol., d'électrol. et de méd. nucléaire*, Nov., 1960, *41*, 645–659.

In craniofacial dysostosis, compressive atrophy of the optic nerve may result from either intra- or pericanalicular hyperostosis; typically, the canal's vertical height is diminished by deformity of the lesser sphenoidal wing. In cases of concurrent oxycephaly, optic atrophy is especially likely to occur because of the added factor of intracranial hypertension.

Evaluation of the optic foramen has some prognostic value, since, if it is intact, the dystrophic process is benign, not only as it concerns the organs of vision but also the skull and brain.

Not all cases of craniofacial dysostosis show the imprint of cerebral convolutions on the calvarium. The authors note that in 1 of their cases a concurrent hydrocephalus prevented the development of these digital impressions.—*Frank A. Riebel, M.D.*

Legré, J., Denizet, D., and Savelli, J. (Marseille, France.) Lacunes craniennes secondaires à un traumatisme de la première enfance. (Cranial lacunae secondary to trauma suffered in early childhood.) *J. de radiol., d'électrol. et de méd. nucléaire*, Nov., 1960, *41*, 667–678.

Localized trauma in early childhood occurs in all cases of cranial lacunae; in 6 of the authors' 7 cases the injury occurred before the age of two. In 2 of the cases the parietal bones were affected as the result of the application of obstetrical forceps with resulting ischemic necrosis; the other 5 gave a history of falls.

The initial pathology largely determines the course; a dural tear is especially important, as it may permit development of a leptomeningeal cyst, porencephaly, or its healing may produce cicatricial retraction between bone and brain through the intermediary of a dense block of fibrous tissue. While usually a true fracture occurs, it is possible to have an intradiploic hemorrhage which causes progressive spreading of the two tables of bone. It is difficult to say when the lacuna develops because frequently there is a latent period between injury and the development of symptoms. In 1 of the cases cited, however, a leptomeningeal cyst apparently developed in a few days.

The typical roentgen findings are a clear lacuna in the cranial bone at the site of the old injury, with the outer table showing extensive exophytic reaction, often appearing like the crest of a helmet; the internal table may possess spicules. Usually the affected half of the skull is the larger, although in 1 of the authors' cases the opposite was true because of brain atrophy. A pneumoencephalogram will show slight dilatation of the ventricle on the affected side and its retraction toward the lacuna.—*Frank A. Riebel, M.D.*

Hurxthal, Lewis M. Pituitary gigantism in a child five years of age: effect of x-radiation, estrogen therapy and self-imposed starvation diet during an eleven-year period. *J. Clin. Endocrinol. & Metabol.*, Mar., 1961, *21*, 343–353. (From: Department of Internal Medicine, The Lahey Clinic, Boston, Mass.)

A case history of pituitary gigantism in a five year old girl is presented. The syndrome began at the age of three, and was studied for eleven years (age five to age sixteen). The syndrome is well documented, and reproductions of impressive skull roentgenograms and photographs of the child are included. Detailed metabolic data are given in tables.

At the age of nine, 2,400 r was administered to the pituitary by rotational supervoltage roentgen therapy. Further therapy was refused. The serum phosphorus and growth rate decreased for a period of about nine months. Further radiation therapy was not given, and estrogens were used in an attempt to control the child's growth. The data show that some further improvement was obtained; however, it was less striking than that following radiation treatment. At the age of twelve the patient placed herself on a starvation diet, and during this time she grew only one-fourth inch. No change in the sella was noted during the period of malnutrition (four years).

The author recognizes the fact that a larger dose of radiation should have been used if possible, and that it should have been employed when the child was first seen at the age of five. The fact that the roentgen therapy gave the best results again demonstrates its value in the treatment of pituitary eosinophilic adenomas. Serum phosphorus determinations are shown to be a useful adjunct in following these patients.—*William K. Littman, M.D.*

Wisoff, Hugh S., and Rothballer, Alan B. Cerebral arterial thrombosis in children; review of literature and addition of two cases in apparently healthy children. *A.M.A. Arch. Neurol.*, Mar., 1961, *4*, 258–267. (Address: 27 Ludlow St., Yonkers 5, N. Y.)

This is a report of 2 cases of cerebral arterial thrombosis in apparently healthy children, both diagnosed by angiography. The first patient died of extensive encephalomalacia and necropsy revealed areas of diffuse vascular disease involving both systemic and cerebral arteries, and a dissecting aneurysm almost totally occluding the lumen of the terminal internal carotid artery and the proximal middle and anterior cerebral arteries on the right. The second case survived with residual hemiparesis and dysphasia; there was considerable narrowing of the supraclinoid portion of the left internal carotid artery seen on angiography. The etiology in this case is obscure although there was a history of head trauma.

The authors also reviewed 27 cases of cerebral thrombosis in children under sixteen years of age, excluding those instances where the etiology and pathogenesis is already well recognized. The incidence seems to be rather low; however, they predict that with the increased use of angiography the disease will prove to be more common.

Males are more often affected and a definite left-sided preponderance is demonstrated. Clinically, an apoplectiform onset was more prevalent and head-

aches and seizures were fairly common. The site of the occlusion is correlated with the degree of recovery and the more proximal occlusions tend to be more benign. The cases of dissecting aneurysm of the internal carotid artery and middle cerebral arteries form the most significant group, although in the remainder of the cases no convincing etiology was found.—*Homero F. Nino, M.D.*

MEYER, H.-ST., BUSCH, G., and DÖRFFEL, E. W. Beitrag zum Problem des "Pseudotumor cerebri" und einer intrazerebralen Verkalkung. (Contribution to the problem of "pseudotumor cerebri" and an intracerebral calcification.) *Fortschr. a. d. Geb. d. Röntgenstrahlen u. d. Nuklearmedizin*, Jan., 1961, *94*, 107–115. (From: Universitäts-Nervenklinik, Röntgenabteilung der Nervenklinik und Universitäts-Geschwulstklinik der Charité in Berlin, Germany.)

The authors take exception to the misused term "pseudotumor cerebri" when it describes any unsolved neurologic condition with increased intracranial pressure. One may find, for instance, the following lesions diagnosed as pseudotumor cerebri: brain abscess, subdural hematoma, aneurysm, atypical migraine, pregnancy encephalitis, thromboangiitis obliterans, tower skull, etc. Nonne coined this term in 1904 to describe subacute or chronic conditions with increased intracranial pressure, and papilledema without demonstrable brain tumor, even at autopsy. (The course is, as a rule, benign with complete remission.) Kehrer proposes to abolish this deceiving pseudodiagnosis and to use instead "increased intracranial pressure of unknown origin." Ketz considers the diagnosis of "pseudotumor cerebri" in certain cases as justifiable, although he agrees with Kehrer that it represents only a clinical syndrome. Some of his 17 observed cases show a normal ventriculogram; others demonstrate a distinct displacement appearance. Zuidema and Cohen, on the other hand, consider the syndrome "pseudotumor cerebri" to represent increased intracranial pressure with papilledema and a normal ventriculogram.

The authors propose to limit the term "pseudotumor cerebri" to the definition of Nonne except for the inclusion of a definite mass displacement visualized with cerebral arteriography and encephalography. To be valid, however, the latter finding must regress at the same time as the clinical symptoms without treatment.

The case report of a patient observed for ten years and fulfilling the above requirements is described. In their discussion the authors mention the very exceptional case of Binswanger, presented in 1912, in which, also, the tumor was not found at operation. Subsequently the patient's symptoms regressed considerably. However after twelve years an autopsy revealed a glioma the size of a hazelnut in the left temporal lobe. In the authors' case, the possibility of a circumscribed encephalitis, brain abscess, parasitic disease or tuberculoma was eliminated. An intracerebral hematoma, calcified after ten years, was believed to have been caused by the needle biopsy undertaken during the operation rather than to have been the cause of the original disease. The possibility of a thorium deposit secondary to thorotrast angiography producing the area of increased tissue density was ruled out with the help of a scintillation counter.—*S. Silvera, M.D.*

WORST, J. G. F. A röntgen reference contact lens, fixed by low vacuum. *J. belge de radiol.*, 1960, *43*, 591–597. (From: University Eye Clinic, Groningen, Holland.)

A contact lens which contains radiopaque markers imbedded in it is described. It is attached to the cornea by a low suction vacuum device. Anteroposterior and lateral roentgenograms are made on which a transparent reference scheme is superimposed. Intraocular foreign bodies are accurately located by this technique.—*David Morse, M.D.*

NECK AND CHEST

ISSA, PHILIPPE. Laryngocèle ventriculaire (à propos de 4 cas). (Ventricular laryngocele [report of 4 cases].) *J. de radiol., d'électrol. et de méd. nucléaire*, Feb., 1961, *42*, 8–16. (From: Hôpital de l'Université Américaine, Service de Radiologie, Beyrouth, Lebanon.)

This rare lesion was first described in 1829 by Larrey as a vesicular or aerial goiter. In 1867, Virchow coined the name "ventricular laryngocele." Thereafter, various names were used for its designation: aerial cyst, diverticulum or aerial hernia of the larynx, monkey pouch or gland.

Description. A laryngocele is an anomalous air sac arising from Morgagni's ventricle or, more precisely, from its anterior vertical extension in the arytenoepiglottic fold, which is 1 cm. long and is called the appendix, pouch, or sacculus ventriculi laryngis. This laryngeal pouch is the vestige of a large bilateral air sac, serving as an oxygen reservoir, which is found in anthropoid monkeys and other mammals and which extends through the thyrohyoid membrane to the base of the neck and sometimes to the axillary regions. In man, this saccule plays an important physiologic role in the lubrication of the vocal cords by its numerous mucous glands. The distention of this saccule results in a true hernia with a wall of its own and a neck attached to the anterior part of the ventricle. Its content is usually air; it may be liquid if drainage is hindered, or purulent with supervening infection, in which case it would be called a laryngopyocele.

Classification. Laryngoceles have been divided by

Lindsay into three categories: (1) internal, expanding in the laryngeal cavity above the superior border of the thyroid cartilage; (2) external, perforating the thyrohyoid membrane and bulging in the neck; and (3) mixed, which has both an external and an internal component. The last two types are the most frequent. Laryngoceles may be bilateral, generally of a different type on each side.

Pathogenesis. Two causes are considered. The first is a congenitally long sacculus with deficient thyroarytenoid muscle action, or a congenital weakness of the thyrohyoid membrane. The second cause is a consequence of increased intralaryngeal pressure which occurs during strenuous and repeated efforts such as singing, shouting, etc. Other contributing factors are local: tumor, granuloma or a cicatrix at the level of the ventricle with trapping of air in the saccule in a valve-like action.

Symptomatology. This varies from a long latency to an acute suffocating attack necessitating a tracheotomy. The most frequent symptoms are: (1) a slight change in voice, dysphonia or aphonia. This symptom is generally present with an internal laryngocele; (2) minimal dyspnea, in the case of slowly progressing enlargement of a laryngocele, or pronounced, even acute, dyspnea when distention is more rapid. It may be continuous, or provoked by effort; (3) the sensation of the presence of an accompanying foreign body with dry cough or the production of white mucoid or purulent secretions. At the acme of an attack, a vomica may occur; (4) rare and slight dysphagia; and (5) pain if the laryngocele is infected.

Clinical and Laryngoscopic Findings. An evocative sign of external laryngocele is a mass located in the anterior triangle of the neck above the thyroid cartilage. It may give an impression of fullness without clear delineation. This is also produced by an internal laryngocele repelling the thyrohyoid membrane. The mass may be big and may extend to the supraclavicular region. It is rounded or lobulated, regular, soft, and tympanic on percussion. It may change in size with coughing and may empty on pressure. When the neck of the sac is obstructed, the mass becomes very hard.

On endoscopic examination of an internal laryngocele, a pinkish rounded mass is seen which is depressible and occupies the lateral portion of the laryngeal vestibule, extending to the aryepiglottic fold and sometimes to the epiglottis or the base of the tongue.

Roentgen Findings. Roentgen examination is important in establishing the clinically suspected diagnosis or in confirming a clinical impression by showing the typical aspect of a laryngocele. On the anteroposterior roentgenogram, a well-defined air shadow will be seen in the para- or intralaryngeal location. The first air collection will be found in the soft tissue of the neck, the second air pocket will be seen through the cervical spine, not extending below the level of C5–C6. On the lateral roentgenogram, the shadow of a laryngocele will be superimposed on the larynx and will extend above it, but its lower margin will not go beyond the level of Morgagni's ventricle. The distance between the hyoid and thyroid cartilages may be increased by compression from the mass, or these structures may show local displacement by it.

Frontal plane laminagraphy will clearly show the two gaseous pouches with a narrow channel connecting them. A fluid level will be seen if the laryngocele is partly filled with secretions.

The author reports 4 cases in full detail with illustrative roentgenograms. In the differential diagnosis, he discusses mucous laryngeal cysts, posttraumatic hemorrhagic cysts of the vocal cords, and congenital cysts from branchial inclusions or cells of the laryngeal saccule. The only curative treatment is the surgical removal of the mass with its wall.—*H. P. Lévesque, M.D.*

Dalith, F. Calcification of the aortic knob: its relationship to the fifth and sixth embryonic aortic arches; a radiological and anatomical study. *Radiology*, Feb., 1961, *76*, 213–222. (Address: Department of Radiology, Government Hospital, Tel-Hashomer, Israel.)

In order to identify the site of preference of calcium deposition in the aortic arch, to investigate the nature of this finding, and to explain its roentgen appearance, laminagraphic examinations in the anteroposterior and latero-oblique projections were made in 27 patients in whom a calcium-dense opacity at the aortic knob was demonstrated on a routine chest roentgenogram. In addition, 100 aortic arch specimens were obtained from consecutive autopsies, fixed in formalin, studied roentgenographically, subjected to gross macroscopic examination, transilluminated and photographed, and studied histologically.

Laminagraphic studies demonstrated that the calcium-dense opacities were practically always situated in the wall of the aorta in the mid portion of the aortic arch opposite the shadow of the pulmonary artery, suggesting that they might be related to and appear as a sequel to the closure of the ductus arteriosus. In the studies of the autopsy specimens of the aortic arch, calcification of the aortic knob was found to be the result of single plaques in the aortic wall located either at the entrance of the ligamentum arteriosum or at the level of the origin of the left subclavian artery, or at both sites. Each of these areas showed a depression on the intimal surface, with increased translucency when viewed by transillumination, indicating thinning of the aortic wall. It may be concluded, therefore, that the preferential deposition of calcium in the aortic arch is related to these structural changes which correspond to the

aortic connections of the sixth and, most probably, the fifth embryonic aortic arches.

The significance of the roentgenologic manifestation "calcified aortic knob," *per se*, for generalized atherosclerosis of the aorta is questioned. Its presence in young persons with patent ductus arteriosus may be accepted as a confirmatory sign of that anomaly. —*Walter H. Jarvis, Jr., M.D.*

SCHEMINZKY, F., and SCHRÖCKSNADEL, H. Einfluss der Radiumemanation auf Herzfrequenz und Blutdruck. (Influence of radium emanation upon pulse and blood pressure.) *Wien. klin. Wchnschr.*, Feb. 17, 1961, *73*, 123–127. (From: Forschungsinstitut der Oesterreichischen Akademie der Wissenschaften in Badgastein und Physiologisch-Balneologisches Institut der Universität, Innsbruck, Austria.)

Observations on the effects of combined hyperthermy and radon inhalation upon pulse and blood pressure in more than 10,000 patients have been made by many competent investigators in the deep thermal galleries of Badgastein. Temperatures were around 42° C.; the relative humidity was 100 per cent and the concentration of the radon about 4.1×10^{-9} curie per liter. The combined effect of humid air at a high temperature and radon inhalation produced in a large number of patients a considerable reduction of strain in blood circulation.

Since such studies in the Badgastein galleries are subject to many variable and often uncontrollable factors, the authors made similar studies under better controllable conditions in the artificial emanatorium of the Innsbruck Physiologic-Balneologic Institute. The pulse and blood pressure of 45 healthy medical students were measured before and after the inhalation of radon (at a concentration of 5×10^{-9} curie per liter) for one hour. Inhalation of this gas at room temperature had practically no effect upon pulse and blood pressure. However, if the room temperature was increased to 41.5° C. and the humidity raised to 90 per cent, it was observed that radon inhalation considerably reduced the strain upon blood circulation produced by the hyperthermic conditions. No explanation of the mechanism of this specific radon effect can be offered at present.—*Otto Glasser, Ph.D.*

VON BRAMANN, CONSTANTIN. The surgical treatment of primary and secondary reflux esophagitis. *Proc. Rudolf Virchow Med. Soc.*, 1960, Jubilee Volume, *99*.

Primary reflux esophagitis is most frequently found in cases of diaphragmatic hiatus hernia. Secondary reflux esophagitis occurs after surgery on the cardiac portion of the stomach, particularly after resection of the cardia for ulcer or carcinoma. The most painful form of reflux esophagitis is observed after anastomosis between the esophagus and the jejunum (esophagojejunostomy).

The numerous operative procedures recommended for treatment of primary and for prevention of secondary reflux esophagitis are described. However, it is also pointed out that the majority of esophagogastric anastomoses do not lead to reflux esophagitis, even without preventive operative techniques. In the author's own series of about 100 cardiac resections, there were only 2 patients who developed reflux esophagitis and these responded to conservative measures.

Even with this low incidence, reflux esophagitis is a real problem to the surgeon, internist and general practitioner because of its severe and disabling symptoms and because of the steadily increasing number of operations on the lower esophagus and cardiac portion of the stomach. The chances for the future development of ways for successfully replacing the esophagus with plastic material are considered to be favorable.—*Franz J. Lust, M.D.*

ABDOMEN

HEALEY, WILLIAM V., RIGGINS, ROBERT C., WHITE, RICHARD L., HABIF, DAVID V., and STEWART, WELLINGTON B. An experimental method for localizing the source of intestinal bleeding. *Surg., Gynec. & Obst.*, Mar., 1961, *112*, 285–288. (From: The Departments of Surgery and Pathology, College of Physicians and Surgeons, Columbia University, New York and Department of Pathology, College of Medicine, University of Kentucky, Lexington, Ky.)

An experimental method for localization of gastrointestinal hemorrhage is described. In this technique, canine red blood cells were labeled with radioactive P^{32}. A series of 3 small Geiger-Müller counters was placed at 8 inch intervals within a Cantor tube passed into the intestine. It was possible to detect local beta radiation with the counter nearest to the bleeding site. There were no false positive readings in the 7 dogs tested. No more than 15 cc. of blood was used in any test segment. Multiple bleeding sites were effectively localized by this method.

The concept is a sound one and, with further technical improvements, the method may find useful clinical application.—*Bernard Loitman, M.D.*

DALLOS, ARTHUR. Complete intestinal obstruction by Meckel's diverticulum. *Proc. Rudolf Virchow Med. Soc.*, 1959, *18*, 76.

A forty-nine year old man with frequent vomiting and severe abdominal pains was admitted to the hospital for a possible intestinal obstruction. A flat roentgenogram of the abdomen confirmed the

mechanical obstruction. After a short period of deflation and decompression, the patient was operated on. The lower ileum was completely obstructed by a kinking which was caused by a sizable Meckel's diverticulum (approximately 2½ inches long). A small bowel resection including the kinking diverticulum was done. The proximal ileum was anastomosed to the cecum.

Meckel's diverticulum represents a part of the omphalomesenteric duct. A free, blind diverticulum to the ileum is the most common form of the anomaly. It usually occurs within one meter of the terminal ileum.

A Meckel's diverticulum is prone to be involved in three types of pathology: (1) infection, (2) intestinal obstruction, and (3) peptic ulcer. Acute diverticulitis is similar to the clinical picture of acute appendicitis. The obstruction can take the form of kinking, torsion, or constriction of the small intestines or, more rarely, of a mobile portion of the colon. Intussusception may occur. A peptic ulcer in a Meckel's diverticulum may be complicated by perforation, obstruction, or hemorrhage. The presence of a Meckel's diverticulum can seldom be diagnosed before operation.—*Franz J. Lust, M.D.*

Elkan, Wolf. Two rare tumors of the ileum. *Proc. Rudolf Virchow Med. Soc.*, 1959, *18*, 81.

Tumors of the ileum are extremely rare, their frequency among abdominal tumors being estimated as less than 1 per cent. They are difficult to diagnose, since the liquid nature of the contents of the small intestine makes obstruction a very late manifestation and the mobility of the small intestine allows them to move about more freely and thus prevents early manifestation of pain due to pressure on neighboring structures. Early roentgen diagnosis is equally difficult because of the irregular pattern and the superimposition of the small intestine.

The first patient reported was a seventy year old female. She had first noticed progressive weakness, loss of weight and appetite, and abdominal distention. Later, nausea and vomiting occurred and she consulted her physician, who discovered a large, fixed mass in the right pelvic region. At operation, a large adenocarcinoma of the ileum was found.

The second case was a sixty year old male who suffered from hypertension (about 200), chest pains, headaches, profuse perspiration, flushing of the face and a feeling of weakness. At first the only positive findings were a sedimentation rate up to 130; however, on roentgen examination of the gastrointestinal tract, an oval filling defect was noted in the right lower abdomen indicating a mass displacing the intestine. At operation, a tumor of the ileum was found; it was a carcinoid of the ileum.—*Franz J. Lust, M.D.*

Margulis, Alexander R., and Mandelstam, Paul. The use of parenteral neostigmine in the roentgen study of the small bowel. *Radiology*, Feb., 1961, *76*, 223–229. (Address: 510 South Kingshighway, St. Louis 10, Mo.)

This paper describes a method of obtaining rapid and good visualization of the small bowel with the use of neostigmine methylsulfate (prostigmin, Roche), which acts as a reversible inhibitor of acetylcholinesterase. This action increases small bowel motility and, therefore, the speed of intestinal transit. Over 3,000 examinations of the small bowel with neostigmine have been completed during a period of ten months at the Mallinckrodt Institute of Radiology. There were virtually no untoward results and in no case was medication or cessation of the examination necessary. No myocardial infarctions, intestinal perforations, or other serious complications occurred that could be attributed to the use of this drug. The contraindications in the dose range used by the authors are: intussusception, volvulus, complete intestinal osbtruction, perforation, peritonitis, and recent myocardial infarction.

An initial pilot study in 107 successive unselected patients who received 0.5 mg. (or 0.75 mg. in patients weighing more than 190 lb.) neostigmine subcutaneously after completion of fluoroscopy of the stomach and duodenum showed that barium had reached the cecum or beyond within one hour in 93 (87 per cent). A subsequent study was done in which 153 patients were given neostigmine as above; another 299 patients were given a placebo (an equal volume of 5 per cent glucose in water) subcutaneously, and another 157 patients received no injection. Neostigmine was shown beyond doubt to speed intestinal transit. In comparison with the control group receiving no injection, the placebo definitely accelerated propulsion of the barium meal, although it was not nearly as effective as neostigmine, and also showed the importance of psychic influences on intestinal motility.

The procedure now followed in routine upper gastrointestinal surveys (in the absence of contraindications) is to give 0.5 mg. of neostigmine (0.75 mg. in patients over 190 lb.) subcutaneously following fluoroscopic examination of the stomach and duodenum, with roentgenograms being taken fifteen and sixty minutes after the injection and, if necessary, later. When detailed studies of the small bowel are desired, roentgenograms are obtained at fifteen, thirty, forty-five, sixty, and one hundred and twenty minutes after administration of neostigmine and at further intervals if necessary.

The authors have been able to diagnose by these means cases of sprue, lymphosarcoma of the small bowel, regional ileitis, adhesions, and involvement of the small bowel by metastatic tumor. The drug does not modify the characteristic morphology and does not alter transit in conditions of disordered motor function.—*Donald N. Dysart, M.D.*

GRIFFITHS, J. D. Extramural and intramural blood-supply of colon. *Brit. M. J.*, Feb. 4, 1961, *1*, 323–326. (From: St. Bartholomew's Hospital, London, England.)

Postmortem injection studies of blood vessels can be misleading due to technical difficulties such as postmortem clotting, spasm and the viscosity of the injection solution. For the studies of the colon reported by the author, the specimens were injected as soon as possible after death or surgical removal. Infusion with a weak ammonia solution or a saline heparin solution prior to injection prevented necropsy spasm and postmortem clotting, respectively. A barium gelatin or a barium methylcellulose mixture was used as the medium for visualization. A series of experiments was performed which demonstrated the anastomoses between the superior and inferior mesenteric arteries via the middle and left colic arteries. They showed that ligation of the inferior mesenteric artery is a feasible procedure. The adequacy of the marginal artery as a collateral channel and the presence of adequate anastomoses between the middle rectal and superior rectal arteries were shown. Submucosal, mucosal and muscular plexuses form an intricate pattern in the wall of the colon. It is important that ligation of the marginal artery at surgery be at or about 2 cm. beyond the site of resection of the colon or ischemia will result.—*David Morse, M.D.*

KHILNANI, MANSHO T. Calcified liver metastasis from carcinoma of the colon. *Am. J. Digest. Dis.*, Mar., 1961, *6*, 229–232. (From: Department of Radiology, Mount Sinai Hospital, New York, N.Y.)

The appearance of the fine, punctate, closely spaced calcifications in necrotic areas of liver metastases from carcinomas of the colon has been well described previously in cases with the metastases usually coming from the sigmoid or rectosigmoid portion of the colon. The present report is mainly concerned with similar metastases from a carcinoma of the right colon, but it does add another case in which the metastases came, characteristically, from the sigmoid.

This type of calcium deposition somewhat resembles the so-called psammoma calcification characteristic of ovarian carcinoma, but it can readily be distinguished from the peripheral ring-like calcification associated with cysts or abscesses of the liver, the multiple discrete calcifications of disseminated tuberculosis or histoplasmosis, and the phleboliths of a hemangioma. The mottled appearance of thorotrast deposition is more diffusely spread through the entire liver and includes the spleen. A primary hepatoma can show calcifications similar to those in a metastasis from the colon but, as these are usually found in young children, the discrepancy in the ages of the two groups makes the differentiation possible.

The calcified metastases from carcinoma of the colon do not indicate any special characteristics of the original tumor in contrast to the instances of calcification within primary gastric tumors that appear to be associated with mucoid types of carcinoma.—*Donald M. Monson, M.D.*

SICHEL, D., WOLFF, R., and EISENBETH, R. (Strasbourg, France.) Dépistage et fréquence des tumeurs benignes de la vésicule biliaire (étude de 20 cas). (Detection and incidence of benign tumors of the gallbladder [study of 20 cases].) *J. de radiol., d'électrol. et de méd. nucléaire*, Feb., 1961, *42*, 17–24.

Among the multiple causes of biliary dyskinesia and noncalculous cholecystopathy, one is particularly disregraded, even ignored, and that is the existence of benign tumors of the gallbladder.

Contrary to present day belief, these tumors are not rare. In less than two years, the authors have diagnosed 20 cases of benign tumors. Kirklin reported an incidence of 8.5 per cent in 17,000 surgical specimens. Jutras, Longtin, and Lévesque have recorded an incidence of 6.8 per cent of cholesterolosis in 2,494 removed gallbladders during a five year period (1951 to 1955).

Many reasons explain why these lesions escaped roentgenologic detection. A small tumor defect may go unrecognized due to the too great opacity of the gallbladder or it may be interpreted as an artifact or, especially, as intestinal gas. A precise roentgen technique is of prime importance. It should include roentgenograms taken before and after a fat meal and in different positions (erect, Trendelenburg, horizontal) with various angles of projection (en face, lateral, oblique, tangential). Gradual compression under fluoroscopic control is most important.

The main criterion in establishing the existence of a tumor is its fixation to the gallbladder wall, thus eliminating the possibility of gas or a stone.

The size of the tumor may vary from a few millimeters to a centimeter. The solitary defect has a rounded and regular contour when it is benign. The authors have not observed concomitant lithiasis. Very often the contour of the gallbladder is dentate, an appearance which corresponds to that of diffuse granular cholesterolosis.

The benign tumors of the gallbladder are usually a product of a hyperplastic cholecystosis. Jutras, Longtin and Lévesque have classified the hyperplastic processes into three main groups: (1) cholesterolosis (diffuse or strawberry gallbladder, solitary or multiple polyps of cholesterolosis), (2) adenomyomatosis, and (3) neuromatosis. If the tumor is not found on the specimen by the surgeon or the pathologist, it is because of faulty technique in the removal of the gallbladder, especially by clamping the fundus.

The authors do not state the total number of removed gallbladders, nor do they say if their 20

cases were confirmed. The roentgen appearance and histologic nature of the tumors are not described. Jutras and his associates have shown the high incidence of lithiasis with these hyperplastic cholecystoses.—*H. P. Lévesque, M.D.*

Lauchenaur, Clara. Zur Frage der Prophylaxe von Biligrafin-Zwischenfällen. (Prophylaxis of biligrafin reactions.) *Schweiz. med. Wchnschr.*, Jan., 1961, *91*, 45–46. (From: Universitätsinstitut für Röntgendiagnostik und Strahlentherapie des Bürgerspitals Basel, und der Pathologisch-anatomischen Anstalt der Universität, Basel, Switzerland.)

Intravenous administration of biligrafin (cholografin) for cholecystography frequently provokes hot flushes, sneezing, cough, urticaria, slight nausea and vomiting. These side effects are believed to be caused by a hypersensitivity to the entire molecule complex of the contrast material when an iodine allergy has been excluded. Severe reactions have become rare, but a case with fatal outcome is reported.

An ambulatory male patient, aged sixty-one, with the diagnosis of gallbladder disease, was referred for intravenous cholecystography to be followed by a gastrointestinal examination. He was cachectic and appeared very sick. After all preliminary tests for iodine sensitivity were made and proved negative, 20 cc. of biligrafin forte was injected intravenously within three minutes. Nausea ensued after the injection of 16 cc., but following a few deep respirations the injection could be completed. Thirty seconds later, however, the patient became very pale and began to have convulsions. This was followed by Kussmaul's respiration and cardiac arrest in systole. Thoracotomy was performed without delay, but cardiac massage proved ineffective.

Autopsy findings included aortic stenosis, coronary sclerosis, multiple myocardial scars, dilatation and hypertrophy of the left and right heart chambers, a patent foramen ovale, arteriosclerosis and atheromatosis of the aorta and its branches, a large adenocarcinoma of the gastric cardia with esophageal stenosis and metastatic spread, hydrops of the gallbladder secondary to an occluding cystic duct calculus and acute as well as chronic generalized congestion, hyperemia of meninges, cerebral edema, and evidence of moderate cerebellar tamponade.

Aortic stenosis may lead to sudden death. In this case, however, the sudden demise was undoubtedly due to the biligrafin injection. Since iodine sensitivity could be excluded, the reaction was believed to be due to calcium imbalance. The aortic stenosis may have caused prolonged stagnation of biligrafin in the dilated left ventricle. Thus, the cardiac musculature could have been suddenly deprived of vital calcium molecules. Recent animal experiments tend to corroborate such a conclusion.

In a series of 180 cases examined after the fatality described above, injection of calcium salts together with an antihistaminic drug was given prophylactically, and the subsequent intravenous administration of biligrafin was done very slowly. This premedication succeeded in preventing side effects. It must be remembered, however, that intravenous medication with calcium salts is contraindicated in patients being treated with digitalis.—*Ernest Kraft, M.D.*

Lamprecht, Werner. Pancreatic cysts in modern surgery. *Proc. Rudolf Virchow Med. Soc.*, 1960, Jubilee Volume, *274*.

The etiology, pathogenesis, symptomatology and diagnosis of pancreatic cysts are discussed. Only pseudocysts—those not lined with secreting epithelium—cause symptoms (usually because of their size) and require treatment.

Only surgical intervention is effective. Various operative procedures are evaluated and a new, improved operation is described which is simple, safe and satisfactory. It consists of a wide anastomosis between the cyst and the posterior wall of the stomach by a transcystic approach. The contents of the cyst—fluid and pancreatic tissue debris—are completely removed and the already existing adhesions between stomach and cyst are utilized in securing the anastomosis. The operation has been done on 8 patients and has resulted in roentgenologically proved fast shrinkage and obliteration of the cyst.

Clinically, it is important to watch for diabetes; its incidence in these 8 patients rose from 12.5 per cent preoperatively to 55.6 per cent postoperatively. —*Franz J. Lust, M.D.*

Gynecology and Obstetrics

Singleton, Edward B., Rosenberg, Harvey M., and Samper, Luis. Radiologic considerations of the perinatal distress syndrome. *Radiology*, Feb., 1961, *76*, 200–212. (Address: Texas Children's Hospital, Houston, Texas.)

The purpose of the present paper is to discuss the roentgen manifestations of the conditions which, in the opinion of the authors, are the sequelae of hypoxia or anoxia in the perinatal period, *i.e.*, directly prior to delivery, during the birth process, or immediately thereafter. These conditions, having a common denominator of anoxia and a common pathogenesis, *i.e.*, increased capillary fragility, constitute the perinatal distress syndrome. A number of them are roentgenologically demonstrable, whereas others are disclosed only at the time of necropsy.

Intracranial hemorrhages are commonly encountered in infants who have suffered from anoxia in intrauterine life or in the neonatal period. Although the degree is seldom severe enough to produce roentgen changes in the skull, intracranial hemorrhage should be suspected in any newborn infant

with respiratory distress and a normal chest roentgenogram.

Infants with hyaline membrane disease are usually born prematurely under circumstances consistent with anoxia, which by increasing capillary permeability may readily allow the effusion of fibrinogen into the alveoli and provide the necessary conditions for the formation of hyaline membranes. The roentgen features are usually characteristic and frequently present before the respiratory difficulties become noticeable.

Whereas hyaline membrane disease is more common in the premature infant, the aspiration syndrome is usually found in the postmature baby, apparently the result of the onset of respiration *in utero* or during passage through the birth canal. The respiratory symptoms are similar to those of hyaline membrane disease; however, the roentgen findings are similar to those in other forms of aspiration pneumonia. Pneumothorax and pneumomediastinum are common complications in the severe cases.

Pulmonary hemorrhage in the newborn may occur in small, clinically insignificant amounts or may at times be massive, resulting in rapid demise. Fetal anoxia is the most probable cause, although this may be complicated by hypothrombinemia or hemorrhagic disease of the newborn, or accompany erythroblastosis fetalis. Roentgenograms of the chest show changes similar to those in infants with the aspiration syndrome.

Localized noninfectious enterocolitis of early infancy may represent damage to the bowel produced by a focal area of vascular insufficiency. The condition may make its appearance at birth in the form of a localized ulceration of the esophagus, stomach, small intestine, or colon. With perforation, complications become obvious. In the absence of perforation, healing gradually occurs and the accompanying cicatricial changes may produce obstruction several weeks later.

Although intestinal atresia is generally accepted as being the consequence of localized incomplete recanalization of the gut between the seventh and eleventh weeks of embryonic life, there is evidence suggesting that some forms result from interruption of the fetal blood supply to the atretic area due to certain anoxic factors. The roentgen features consist of gaseous distention of the intestine promixal to the site of obstruction and multiple air-fluid levels, usually on upright or decubitus roentgenograms.

The livers of infants who have suffered from anoxia may show changes which are apparently unique to perinatal distress. These anoxic changes are not demonstrable by roentgenographic methods but serve to illustrate the danger of anoxia to the fetal organs. Hemorrhages into the adrenal gland may also result from anoxia and the consequent increase in capillary permeability. Calcification in the adrenal glands of older otherwise normal children probably represents the reparative end result of this condition. —*Walter H. Jarvis, Jr., M.D.*

GENITOURINARY SYSTEM

RUTNER, ALVIN B., and SMITH, DONALD R. Renal papillary necrosis. *J. Urol.*, Apr., 1961, *85*, 462–470. (From: The Division of Urology, University of California School of Medicine, San Francisco, Calif.)

Renal papillary necrosis is an uncommon lesion involving one or both kidneys. It is almost always associated with urinary tract infection and the patient may have a concomitant diabetes mellitus, obstructive uropathy, or chronic interstitial nephritis. In some instances, the disease has been associated with overdosage of phenacetin. The clinical course may be acute, subacute, or chronic. The primary pathologic lesion is a coagulative necrosis of one or more renal papillae with more or less involvement of the medulla. The cortex is not involved in the necrotic process but may show pathologic features of chronic nephritis secondary to the papillary disease. When associated with phenacetin abuse, the kidneys show diffuse interstitial fibrosis with a lymphocytic cellular infiltrate and with irregular contraction of the renal parenchyma.

A roentgen diagnosis can be established in the majority of subacute and chronic cases. The roentgen finding consists of a diffuse, hazy outline of the minor calyces in the early stages. Subsequently, as the disease progresses, there is evidence of sinus tract formation and the contrast medium may be seen in arc shadows or ring shadows adjacent to the minor calyces. These changes are observed both on the retrograde and intravenous pyelograms. They tend to be progressive and, in the final stages, show evidence of clubbing of the calyces with medullary necrosis and small contracted kidneys. During the course of the illness, the patient frequently passes necrotic tissue in the urine.

The prognosis is generally poor. Vigorous conservative management is indicated in most instances.

Ten figures consisting of anatomic drawings, reproductions of intravenous and retrograde pyelograms, and pathologic sections illustrate 4 case histories presented in this article.—*George W. Chamberlin, M.D.*

KLEIN, RICHARD L., and MCCHESNEY, JOHN A. Hypertension secondary to aneurysm of the renal artery: report of a case of long duration cured by nephrectomy. *Ann. Int. Med.*, Feb., 1961, *54*, 292–300. (From: Department of Medicine, Washington University School of Medicine, Barnes Hospital, St. Louis, Mo.)

The case of a twenty-six year old female is presented to illustrate an apparent cure of long-standing hypertension associated with an aneurysm of the left renal artery. The patient had been in excellent health until 1944, when, at the age of thirteen, she suddenly developed headaches accompanied occasionally by nausea and vomiting. The persistence of

these symptoms necessitated hospitalization, at which time her systolic blood pressure was 180 mm. Hg. She was treated with medication and received symptomatic relief. In 1951 she was admitted to another hospital for evaluation of hypertension. All laboratory tests, performed at this time, were within normal limits.

Urinary function tests, medications and the results are given for hospital observations in 1952 and 1956. These were during her two pregnancies, the first being a spontaneous delivery of a normal child at seven and one-half months' gestation and the second pregnancy terminating with the delivery of a seven month stillborn.

In 1957, differential renal function studies were performed, utilizing bilateral ureteral catheters. These showed a reduced glomerular filtration rate per nephron in the left kidney, compatible with extrinsic renal arterial disease. These observations were significant in that the combined glomerular filtration rate of both kidneys was within normal limits. An excretory urogram showed decreased concentration of the opaque medium by the right kidney and normal concentration on the left. Both kidneys were of normal size and shape.

An aneurysmal dilatation of the inferior branch of the left renal artery was demonstrated by translumbar aortography.

The patient has been normotensive for eighteen months following removal of the left kidney.— *John D. Hummel, M.D.*

Winter, Chester C. Advances in the radioisotope renogram test. *J. Urol.*, Apr., 1961, *85*, 683–687. (From: The Department of Surgery, Division of Urology, Ohio State University Health Center, Columbus, Ohio.)

Since its introduction in 1956, radioisotope renography has proved its value as a screening and diagnostic procedure in the evaluation of a variety of urinary tract diseases. The renogram has received widest clinical acceptance in the evaluation of differences in renal vascular supply in the hypertensive patient in whom a nonrenal hypertensive etiology has been eliminated. The study is of value in detecting and following obstruction in the upper urinary tract; an ideal way of following a small ureteral calculus is with periodic plain roentgenograms and renograms. These show the position of the stone as well as the function and drainage of the involved kidney without the added exposure and risk of repeated excretory urograms. By renography one can also readily differentiate acute renal failure from complete obstructive uropathy in the anuric patient within the first forty-eight hours.

The author emphasizes the importance of attention to details and proper instrumentation in performance of the study. He feels that most nondiagnostic radioisotope renograms result from improper technique rather than from an inherent deficiency in the procedure itself. Hippuran I^{131} presently seems to be the test agent of choice because it is removed at a rapid rate from the blood exclusively by the kidneys.

By the addition of a third set of instruments to the dual renogram unit for monitoring the chest or any other highly vascular area, an estimation of the rate of blood clearance of hippuran I^{131} may be otbained. The author believes that this blood clearance curve is helpful in estimating quantitative total renal function.

Four short case presentations illustrate the clinical usefulness of this study.—*George W. Chamberlin, M.D.*

MacLaurin, John C., and Arneil, Gavin C. Phaeochromocytoma causing ureteric obstruction in a child. *Lancet*, Feb. 25, 1961, *1*, 426–429. (From: The Department of Child Health, University of Glasgow, and The Royal Hospital for Sick Children, Glasgow, Scotland.)

The view is now taken that any adrenalin- or nonadrenalin-secreting tumor, irrespective of its site of origin, should be called a pheochromocytoma. Only 5 per cent of all reported cases of this tumor have been in children and, in them, 15 per cent have originated outside the adrenal gland.

This case report is of a twelve year old girl with an eight month history of intermittent headaches, one month of anorexia and some weight loss, and three recent episodes of left abdominal pain associated with nausea and vomiting, but no urinary symptoms, paroxysmal flushing, sweating or palpitation.

Investigative studies revealed that the facies and general demeanor vaguely suggested thyrotoxicosis, though exophthalmos and tremor were not present. Blood pressure on admission was 185/125 mm. Hg. There was bilateral papilledema, proteinuria, a four- to sixfold increase in the catecholamine content of the urine, an erythrocyte sedimentation rate of 59 mm. in the first hour and a solitary gallstone. Intravenous pyelography disclosed a nonfunctioning left kidney and at cystoscopy the ureteral catheter could not be passed more than 2 cm. up the left ureter. The paroxysmal nature of the hypertension became apparent with observation, but the Regitine test was equivocal. Notwithstanding, the correct diagnosis was suggested preoperatively.

At surgery, a tumor mass was found encircling the left ureter about 2 cm. above the bladder, but it was mainly around the lower inch of the aorta, the bifurcation and the left common iliac artery. The bladder wall was not involved. All tumor tissue was removed macroscopically with considerable difficulty. The left kidney and adrenal gland were also excised, the former because the degree of hydronephrosis was greater than expected, and the latter because clamping of the left renal vein caused an immediate drop in blood pressure. By palpation the right adrenal was

normal, and the left subsequently proved to be normal also. The postoperative course was satisfactory and her full recovery dramatic.

The problem of malignancy arises often since many of these tumors, as in this case, appear locally invasive. The authors concur that distant metastasis appears to be the only reliable criterion of malignancy, with such a complication present in about 2.5 per cent of cases.

It is speculated that the site of origin of this tumor was probably the organ of Zuckerkandl. Abdominal symptoms have been noted as being the rule in these cases. In the only other known case presenting with a nonfunctioning kidney, the tumor arose in the bladder.—*Donald M. Monson, M.D.*

NERVOUS SYSTEM

SCHOBER, R. Zystische Bildungen der häutigen Rückenmarkshüllen. (The formation of cysts in the coverings of the spinal cord.) *Fortschr. a. d. Geb. d. Röntgenstrahlen u. d. Nuklearmedizin*, Jan., 1961, *94*, 116–129. (From: Universitätsstrahleninstitut, Homburg-Saar, Germany.)

The development of cysts in the space between the spinal cord and the spine produces symptoms of a space occupying lesion similar to disk herniation or to a tumor. These cysts are differentiated as intradural, extradural or epidural-perineural according to their location.

The author's series comprises 247 cases studied by myelography of the cervical region (49 cases), the thoracic region (36 cases), and the lumbosacral portion of the spine (162 cases). Twenty-one cases showed signs of epidural-perineural cysts, 16 in the lumbosacral region and 5 in the cervical region. These cysts are connected with the subarachnoid space and fill with the contrast medium as do diverticula. Their size varied from that of a peppercorn to a peanut. In none of the 21 cases could the neurologic symptoms be correlated with the myelographic findings. Eleven of the 16 cases of cysts in the lumbosacral region showed, in addition, evidence of herniation of the nucleus pulposus and in all these cases the cysts were below the level of the herniation.

In analyzing these findings, and reviewing the anatomy and embryology of the spinal cord, nerve roots and dural coverings, the author arrives at the conclusion that developmental abnormalities are a factor responsible for these cysts, a theory which seems especially plausible when one considers the shifting of the ganglia from the intradural to the extradural space and back again as observed in the 24 mm., 34 mm. and 54 mm. fetus. Also, one must take into consideration the disproportionate development in the length of the spine in relation to its contents from the time the fetus reaches 34 mm. For instance, root pouch of unusual length and varied width may develop if the coordination of length development to the movement of the ganglia is impaired.

A second factor in the development of epidural-perineural cysts is the pressure fluctuation of the cerebrospinal fluid, which is elevated when the pressure in the veins is raised thus causing decreased fluid absorption. This is especially true in herniation of the nucleus pulposus or other space occupying lesions in the extradural space which causes a localized circulation disturbance.

As a rule, these not infrequently observed epidural-perineural root pouch cysts have no clinical significance.—*S. Silvera, M.D.*

SKELETAL SYSTEM

INNES, JAMES, and NEWALL, JOSEPH. Myelomatosis. *Lancet*, Feb. 4, 1961, *1*, 239–245. (From: Departments of Medicine and Radiotherapy, University of Edinburgh and Royal Infirmary of Edinburgh, Scotland.)

One hundred eighteen cases of myelomatosis were reviewed in a study of the natural history of the disease. In this series the ratio of men to women was about 3 to 2 and the disease developed after the age of fifty in 80 per cent of the cases. The disease results from an abnormal proliferation of reticulum cells in or outside the bone marrow and is manifested by four different varieties.

Solitary Myeloma (46 cases). The plasma cell proliferation may start in a single bone, giving rise to a solitary myeloma. This eventually shows as a local swelling of bone which is often painless. A solitary osteolytic defect is seen roentgenographically, with no evidence of disease in the rest of the skeleton. The three year survival rate in this group was 32 per cent. The focus of plasma cell infiltration may remain localized for long periods of time. Eventually, multiple foci appear elsewhere in the skeleton. In this latter stage it is indistinguishable from multiple myeloma.

Multiple Myeloma (119 cases). The growth of multiple small intramedullary tumors results in disseminated osteolytic defects in bone, with the spine, skull, ribs and pelvis being most often affected. Anemia is more common in this group than in patients with the solitary variety. Myelomatous infiltration was reported in bone marrow studies of all but 8 of 96 patients thus examined. The three year survival rate was 5.3 per cent. No case survived for five years. Bronchopneumonia, severe anemia, uremia and cardiac failure were the most frequent terminal events.

Diffuse Myelomatosis (17 cases). A diffuse infiltration of the bone marrow occurs without discrete tumor masses. Diffuse osteoporosis may be seen roentgenographically but there are no diagnostic roentgen changes. Gradual onset of anemia is the usual reason for examining these patients. Once

severe anemia is manifest these patients deteriorate fairly rapidly, without remission, and are unaffected by treatment. The course of the disease is like that in severe aplastic anemia and the patients often succumb to pulmonary infections.

Extramedullary Plasmacytoma (6 cases). This is the most rare form of myelomatosis. The first manifestation is soft tissue tumor formation, which may later develop bony involvement.

The laboratory findings in these conditions are analyzed. Although an elevated erythrocyte sedimentation rate was present in 85 per cent, the rate was normal in the remaining 15 per cent. High readings were most common in the generalized form. Hyperglobulinemia was present in 70 per cent of the 118 cases tested and this was a result of an increase in the gamma component. Bence Jones protein was found in 35 per cent. The anemia is almost always normochromic and normocytic. There is a tendency to rouleau formation. Increased plasma cells are rarely seen. In general, an examination of the peripheral blood smear is of little diagnostic value.—*David Morse, M.D.*

Unander-Scharin, Lars. Melorheostosis; report of a case. *Acta orthop. scandinav.*, 1960, *30*, 101–106. (From: The Orthopaedic Clinic, Harnosand, Sweden.)

Melorheostosis is a very rare disease of bone first described by Leri and Joanny in 1922. It is characterized by continuous aching pain and limitation of motion, usually in one lower extremity. Presumably, the disease begins prior to birth or in early childhood and progresses very slowly. It may be associated with scleroderma or other soft tissue disturbance.

The roentgen features have been compared to liquid drops of wax which run down the long bones and are localized along the vessels and nerve paths. In small bones the changes are streaky or resemble ink blots. They have a "marblebone" appearance, but osteopetrosis can be differentiated because of its generalized nature.

The author describes a typical case of melorheostosis, which was followed for sixteen years. It was limited to the knee, lower leg, and foot of a patient who eventually underwent surgery for removal of a large mushroom-like exostosis from the medial femoral condyle.—*Arch H. Hall, M.D.*

Naide, Meyer, and Schnall, Charles. Bone changes in necrosis in diabetes mellitus; differentiation of neuropathic from ischemic necrosis. *A.M.A. Arch. Int. Med.*, Mar., 1961, *107*, 380–383. (From: Department of Medicine, Woman's Medical College of Pennsylvania and the Department of Medicine, Albert Einstein Medical Center, Philadelphia, Pa.)

The roentgen changes of osseous structures are of prime importance in differentiating ischemic from neuropathic lesions in the feet of diabetic patients. This differentiation is important because the treatment varies. In the neuropathic lesion, the treatment can often be limited to a toe amputation or incision and drainage, while in an ischemic lesion a leg or midthigh amputation is often necessary. Rarefaction, lysis or destruction of bone in a diabetic foot is often indicative of neuropathy and evidence of adequate blood supply, primary or collateral. On the contrary, in ischemic necrosis the circulation is impaired; therefore, no catabolism takes place and no bony changes occur.

There is a better prognosis in a diabetic patient with a soft tissue lesion of a foot if there is roentgen evidence of bone changes, indicating neuropathy, than if ischemic tissue necrosis is present and the bone is intact.

Two cases of diabetic patients were presented to illustrate the types of necrosis. The first patient had extensive bone destruction at the metatarsophalangeal joints and soft tissue necrosis secondary to diabetic neuropathy. Treatment was debridement. The lesion healed in six weeks indicating that the bone changes were neuropathic and not due to osteomyelitis. The second patient had the usual soft tissue ischemic necrosis typical of diabetes with arteriosclerosis but without roentgen evidence of bone changes. Because of severe pain and extension of necrosis on the foot, amputation at the midthigh was required.—*Jose Amorocho, M.D.*

Hansen, H.-J., and Ullberg, S. Uptake of S^{35} in the intervertebral discs after injection of S^{35}-sulphate. An autoradiographic study. *Acta orthop. scandinav.*, 1960, *30*, 84–90. (From: The State Veterinary Institute and the Department of Pharmacology, Royal Veterinary College, Stockholm, Sweden.)

Radiosulphate (S^{35}) was injected intraperitoneally into newborn piglets which were sacrificed at intervals up to sixteen days. Autoradiographs of sagittal sections of the spine were obtained to secure data regarding metabolic alterations in different morphologic structures.

The S^{35} concentrated in the epiphyseal cartilage, the inner zone of the annulus fibrosus, and the periphery of the nucleus pulposus. As a probable expression of synthesis of the sulphomucopolysaccharides, the incorporation of S^{35} at these sites accords closely with inferences deduced from morphologic features. Tissue layers which form the periphery of the nucleus and the perinuclear portion of the annulus represent the "growth zone" of the disk where fibroid or chondroid metamorphosis of the nucleus takes place.—*Arch H. Hall, M.D.*

Andrén, Lars, and Wehlin, Lennart. Double-contrast arthrography of knee with horizontal roentgen ray beams. *Acta orthop. scandinav.*, 1960, *30*, 307–314. (From: Roentgendiagnostic Department of the University of Lund, Malmo Allmanna Sjukhus, Malmo, Sweden.)

By employing a slight variation in the technique of double contrast arthrography of the knee, the authors have been able to demonstrate 62 of a total of 66 surgical meniscus ruptures. No false positives were obtained.

The technique is as follows: (1) The direction of the plateau is marked on the skin under fluoroscopic control; (2) the joint is aspirated under local anesthesia and 10 cc. of aqueous contrast medium plus an adequate amount of air is injected until the joint feels distended; (3) the patient walks about the room and flexes his knee several times; (4) the patient is placed on his side with the meniscus to be examined uppermost, and a firm pad is placed under the distal end of the femur with a small sandbag on the ankle to separate the joint; (5) film cassettes are placed against the knee and a horizontal roentgen-ray beam is used with a long film focus distance; and (6) the leg is rotated 10 to 15 degrees between exposures to show all parts of the meniscus. Additional views may be made in standard projections with a vertical roentgen-ray beam.

This method requires neither traction apparatus nor the presence of an assistant, and the dangers inherent in the knee-stretching procedures are eliminated. If air is injected first, one seldom gets extravasation of contrast medium into surrounding tissues. The authors agree that the value of any procedure varies with the skill and experience of the examiner, but they have found this technique to be fast, easy, and highly accurate in their hands.—*Arch H. Hall, M.D.*

Blood and Lymph System

Mones, Robert. Vertebral angiography; an analysis of 106 cases. *Radiology*, Feb., 1961, *76*, 230–236. (Address: The Mount Sinai Hospital, Fifth Ave. and 100th St., New York 29, N. Y.)

The purpose of this report is to evaluate vertebral angiography as a diagnostic method in neurology and is based on 106 successful angiograms obtained in a two year period at the Mount Sinai Hospital in New York. A total of 114 attempts at direct vertebral angiography were made, 80 of which were successful. Inadvertently, 14 vertebral angiograms were obtained during the performance of routine carotid angiography and 12 during attempts at indirect filling in 37 patients. The indications for this examination were: subarachnoid hemorrhage; posterior cerebral artery disease; and either vascular disease or neoplasm of the posterior fossa. Fourteen transient complications were seen in the entire series of 128 patients with both successful and unsuccessful direct vertebral angiography. The 37 patients in whom indirect filling was attempted had no complications. Only one permanent complication occurred—an increase in the organic mental syndrome and visual field defect previously present.

Approximately one-third of the studies showed abnormalities. Of the 32 patients with a final diagnosis of basilar artery disease (proved or suspected), 16 had abnormal vertebral angiograms with 11 showing either narrowing or occlusion of a major artery and 5 showing some anomaly, such as an aneurysm or anomalous arteriovenous connection. Sixteen of the 30 patients with a final diagnosis of a tumor had abnormal angiograms. There were 22 posterior fossa tumors and 13 of these showed abnormal angiograms, while 3 of the 8 patients with supratentorial tumors had positive angiograms. While pneumoencephalography is the method of choice for diagnostic evaluation of posterior fossa tumors, incomplete filling or lack of filling of the ventricles may indicate the necessity for veretebral angiograms to attempt further localization. These angiograms may help by showing: (a) tumor stains, which give a good approximation of the position, size and, at times, the histology of the tumor; (b) deviation of an artery, sometimes indicating whether a tumor is intra- or extramedullary; and (c) the presence or absence of an aneurysm, which may act as a mass lesion.

The author feels that the amount of information gained from vertebral angiography is of value as a positive diagnostic test and as a means of ruling out with reasonable certainty certain vascular diseases, such as aneurysm, arteriovenous anomaly, or occlusive disease of the arteries. With care and experience these studies can be done, without undue risk, in patients suspected of having disease in the distribution of the posterior circulation.—*Donald N. Dysart, M.D.*